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Departamento de Ciências Médicas

Ana Rita Barbosa Marques

Estágio na Lenitudes Medical Center & Research – Gestão de Risco

Internship in Lenitudes Medical Center & Research – Risk Management

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Relatório apresentado à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Biomedicina Farmacêutica, realizado sob a orientação científica do Professor Doutor Francisco Luís Maia Mamede Pimentel, Diretor Clínico da Unidade de Saúde Lenitudes Medical Center & Research.

“*Sê todo em cada coisa. Põe quanto és no mínimo que fazes."*

Ricardo Reis

o júri

Presidente	Professor Doutor Bruno Miguel Alves Fernandes do Gago Professor Auxiliar Convidado, Universidade de Aveiro
Vogal - Arguente Principal	Professora Doutora Maria Joana da Costa Gomes da Silva Professora Adjunta, Universidade de Aveiro
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agradecimentos

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O meu profundo e sincero agradecimento a todos.

palavras-chave

Biomedicina Farmacêutica, Lenitudes Medical Center & Research, Gestão de Risco, Farmacovigilância, Eventos Adversos, Investigação Clínica

resumo

O presente documento descreve o estágio curricular realizado na clínica *Lenitudes Medical Center & Research,* localizada em Santa Maria da Feira, que decorreu desde 1 de setembro de 2015 até 31 de maio de 2016. Este estágio foi realizado no âmbito do segundo ano do Mestrado em Biomedicina Farmacêutica da Universidade de Aveiro e teve como objetivos a aquisição de competências técnicas, experiência e consolidação de conhecimentos nas áreas de Gestão de Risco e Farmacovigilância. Para além da aquisição de conhecimentos teóricos, este período de estágio foi fundamental para o desenvolvimento de um conjunto de aptidões sociais e pessoais que contribuíram para o meu crescimento profissional dentro da instituição de acolhimento.

O estágio focou essencialmente tópicos relacionados com a Gestão de Risco, envolvendo a elaboração do Manual de Gestão de Risco da unidade, bem como relatórios periódicos de monitorização de eventos adversos associados à radioterapia. Adicionalmente, durante o estágio foram realizadas atividades de carácter multidisciplinar relacionadas com processos iniciais de investigação e *medical writing*.

Esta foi uma experiência bastante enriquecedora, de grande valor a nível profissional, pessoal e social, que me permitiu atingir os principais objetivos estabelecidos.

keywords

Pharmaceutical Biomedicine, Lenitudes Medical Center & Research, Risk Management, Pharmacovigillance, Adverse Events, Clinical Research

abstract

This document describes an internship carried out in the healthcare unit Lenitudes Medical Center & Research, located in Santa Maria da Feira, held from 1st September 2015 until 31st May 2016. This internship was performed as part of the second year of the Master in Pharmaceutical Biomedicine at the University of Aveiro, aiming to acquire technical skills and experience in Risk Management and Pharmacovigilance, as well as to consolidate previous knowledge. Besides the acquisition of theoretical knowledge, this training period was paramount for the development of a number of social and personal skills that contributed for my profissional growth within the host institution.

The training mainly focused in topics related to Risk Management, involving the preparation of the Risk Management Manual of the unit and adverse events monitoring periodic reports associated with radiotherapy. Additionally, during the internship were conducted multidisciplinary activities related to initial processes regarding research and medical writing.

This internship was a very enriching experience with great value on a professional, personal and social level, that allowed me to achieve the main objectives established.

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List of Abbreviations:

AE	Adverse Events
ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
AIDS	Acquired Immunodeficiency Syndrome
APDH	*Associação Portuguesa para o Desenvolvimento Hospitalar* (Portuguese Association for Hospital Development)
CEC	Commission of the European Communities
CF	Contributing Factors
CHKS	Caspe Healthcare Knowledge Systems
CNS	Central Nervous System
CRO	Contract Research Organisation
CT	Computerized Tomography
CTCAE	Common Terminology Criteria for Adverse Events
DGS	*Direção Geral de Saúde* (Health Direction)
EMA	European Medicines Agency
EORTC	European Organization for Research and Treatment of Cancer
ERS	*Entidade Reguladora da Saúde* (Regulatory Authority of Health)
EU	European Union
FMEA	Failure Mode and Effect Analysis
GVP	Good Pharmacovigilance Practice
GCP	Good Clinical Practice
HazOP	Hazard Operability Analysis
ICH	International Conference on Harmonisation
ICPS	International Classification for Patient Safety
INFARMED	*Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.* (National Authority of Medicines and Health Products, I.P.)
IOM	Institute of Medicine
IRS	Incident Reporting System
ISO	International Organization for Standardization
JCAHO	Joint Commission on Accreditation of Healthcare Organisations
LASA	Look-Alike Sound-Alike
Lenitudes MC&R	Lenitudes Medical Center & Research
MD	Medical Devices
MSCA	Marie Sklodowska-Curie Actions
NCI	National Cancer Institute

NPSA	National Patient Safety Agency
PBL	Problem-Based Learning
PC	Proximate Cause(s)
PET	Positron Emission Tomography
PHA	Preliminary Hazard Analysis
PL	Package Leaflet
PRAC	Pharmacovigilance Risk Assessment Committee
RCA	Root Cause Analisys
R&D	Research & Development
RISE	Research and Innovation Staff Exchanges
RTOG	Radiation Therapy Oncology Group
SAE	Serious Adverse Event
SINAS	*Sistema Nacional de Avaliação em Saúde* (National Health Evaluation System)
SNF	*Sistema Nacional de Farmacovigilância* (National Pharmacovigilance System)
SOP	Standard Operating Procedure
SmPC	Summary of Product Characteristics
SPECT	Single Photon Emission Computed Tomography
USA	United States of America
UK	United Kingdom
WHO	World Health Organization

1. Introduction

The present document constitutes a report about my curricular internship within the scope of the Master's Degree in Pharmaceutical Biomedicine of University of Aveiro. This internship was performed in Lenitudes Medical Center & Research (Lenitudes MC&R), in Santa Maria da Feira, and started in September 1st 2015 and ended in May 31st 2016.

The activities developed during the internship, as well as the learning outcomes and skills acquired during this period, were related to risk management and pharmacovigilance, including a proposal for the creation of tools for reporting of Adverse Events (AE) associated with clinical practice. Nevertheless, were also carried out activities in other areas such as quality management, through the collaboration in the development of Standard Operating Procedures (SOPs), project management, medical writing and other tasks related to clinical research.

1.1 Objectives

The objectives for this on-the-job experience at Lenitudes MC&R were defined in the beginning of the internship and divided into three main areas described below:

- The goals required to conclude the master's degree:
  - To improve the knowledge and skills in Pharmacovigilance and Risk Management;
  - To acquire knowledge about the procedures to increase patient safety, by developing tools for reporting of AE associated with chemotherapy and radiotherapy treatment;
  - To collaborate in SOPs' developing;
  - To be familiarized with national and international regulatory legislation applicable to pharmacovigilance and risk management in healthcare units;
  - To know the International Organization for Standardization (ISO) standards applicable to risk management;
  - To face the healthcare market and the reality within a healthcare unity.
- The objectives related to collaboration on the projects and work within the host company:
  - To be integrated within the clinic's projects;
  - To collaborate on documentation organization and record;

- To get knowledge about the different types of incidents which can occur in a clinical unit with the Lenitudes MC&R's characteristics;
- To observe how communication flows throughout the various sectors within a healthcare unity.

- The aims associated to my personal development:
  - To contact with the clinical environment and adapt to professional life;
  - To understand the applicability of the knowledge and skills developed during academic training;
  - To recognize my difficulties and strengths and improve them;
  - To develop personal and professional skills, such as time management, communication skills (verbal and written), responsibility, autonomy, critical thinking and problem solving.

1.2 Host Organization Portrait

As mentioned above, my curricular internship occurred in a subunit of Lenitudes SGPS company – Lenitudes MC&R. Lenitudes SGPS is a holding company located in Lisbon, which comprises the administration department, general management, project management and legal support of other companies related to health services. Lenitudes SGPS embraces the following units (figure 1 and 2) (1):

- Lenicare – a radiotherapy unit located in Évora, constituting a public-private partnership between the Lenitudes and Hospital Espírito Santo;
- Lenitudes MC&R – my host company, that started being constructed right after Lenicare, in Santa Maria da Feira;
- HPP Molecular Medicine unit (Porto);
- LMN Nuclear Medicine (Braga)
- Surgical hospital (Setúbal) and Hospital (Portimão) – units which will be developed after Lenitudes in Santa Maria da Feira has opened and started operating.

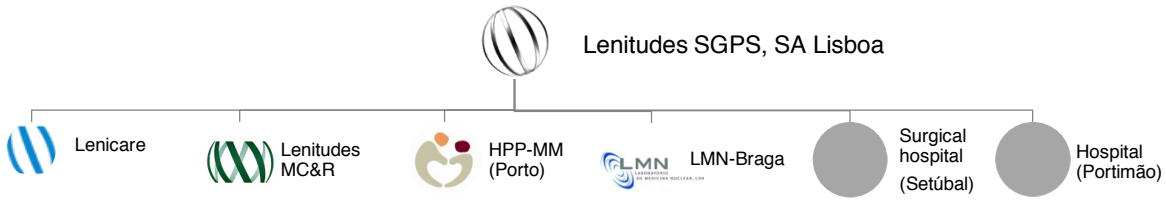


Figure 1 - Lenitudes SGPS Representation and its clinical units (1)

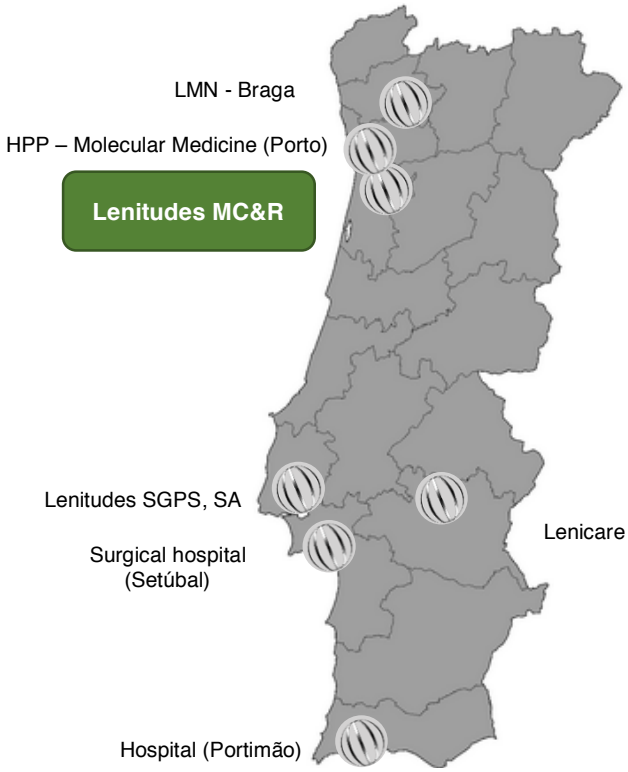


Figure 2 - Lenitudes units' location (1)

1.2.1 Lenitudes MC&R

The Lenitudes MC&R is a healthcare unit, with focus on the treatment of cancer, which belongs to Lenitudes' group, being administered by some members of this holding company. Prof. Francisco Pimentel, my training supervisor, is responsible for Lenitudes MC&R's clinical leadership.

The internal structure of the company is represented in figure 3 (1)**.** In December 2015, the Lenitudes' structure was expanded with the acquisition of HPP Nuclear Medicine unit (Porto) and LMN-Braga, enhancing its resources and its operation area. HPP Nuclear Medicine Units are operating since 12 years ago, having a high number of patients, providing the following diagnostic and therapeutic exams (1):

- Gallium scintigraphy;
- Cerebral perfusion scintigraphy;
- Myocardial perfusion scintigraphy;
- Bone scintigraphy;
- Scintigraphy lung ventilation / perfusion;

- Renal scintigraphy;
- Thyroid scintigraphy;
- Positron Emission Tomography (PET) or PET/Computerized Tomography (PET/CT);
- Single Photon Emission Computed Tomography (SPECT);
- Brain SPECT with Ceretec™ or Neurolite™;
- Brain SPECT imaging with DaTSCAN;
- Therapeutic Iodine - 131 with patient admission.

Beyond this, there are some services that are performed by outsourced companies, such as:

- Human resources for radiotherapy (except specialist physicians);
- Cleaning and hygiene;
- The laundry and the waste management services;
- The sterilization of the surgical and medical instruments and devices.

The activities developed during my internship may be included in the Quality/Risk Management department (represented in figure 3 in red color), which is transverse to Lenitudes SGPS company. Additionally, I also performed some Research and Development (R&D) activities in the area of project management and medical writing (also represented in figure 3 in red color).

This healthcare facility located in Santa Maria da Feira (figure 4) provides a range of clinical services that extend from the diagnostic techniques to clinical treatments. The center has several medical offices and nursing rooms, chemotherapy and preparation of cytostatics rooms, surgical and recovery rooms, research laboratories, radiotherapy rooms, imaging and nuclear medicine. Figure 5 is a sketch of the Lenitudes, with the areas and services it has to offer:

- Nuclear medicine – with two different equipment from General Eletrics, new PET/CT – Discovery IQ ® – and one *g*amma camera SPECT – Discovery NM360 ® –, Lenitudes MC&R has the ultimate technology. The equipment PET/CT is only available in few places worldwide, offering a better image in less time with a much lower dose of radio drugs.

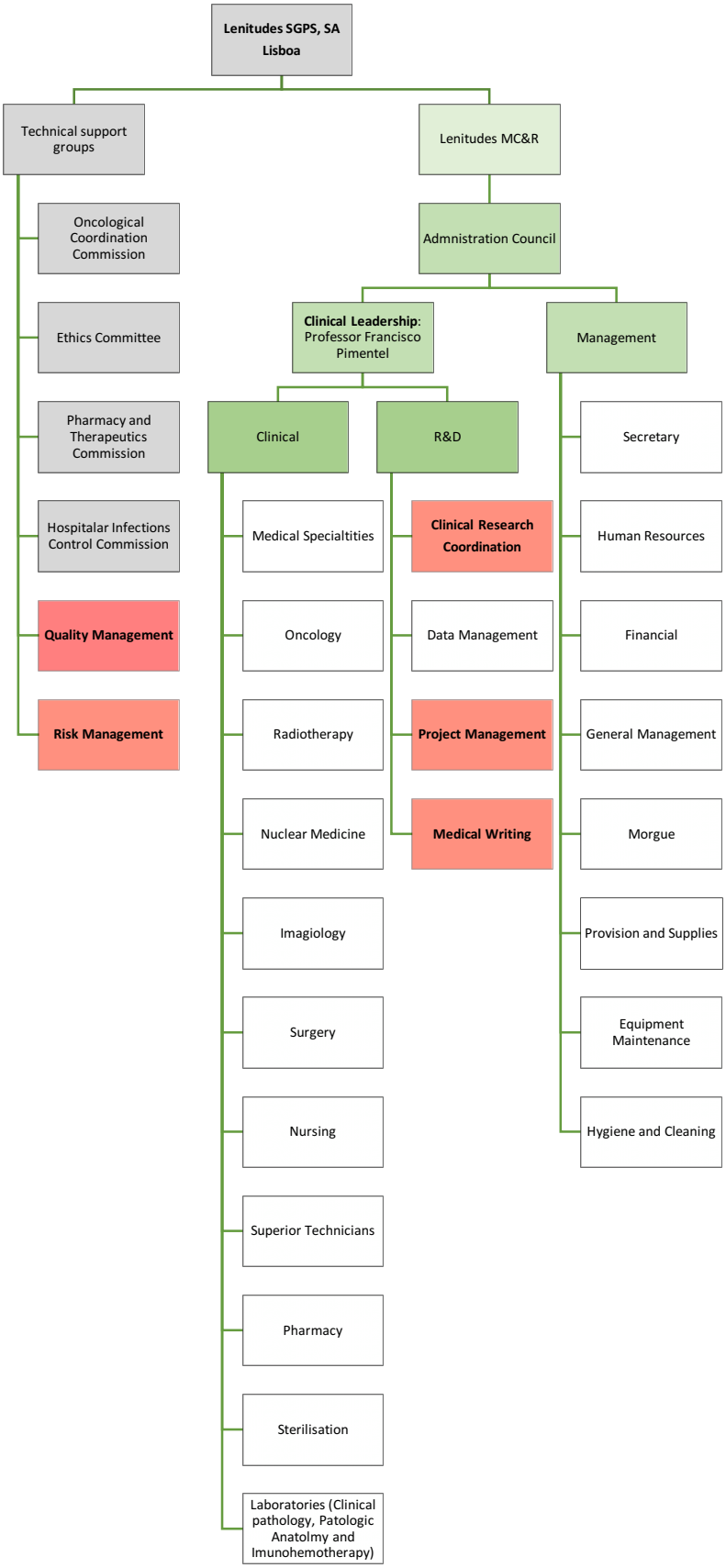


Figure 3 - Lenitudes MC&R organisation chart's proposal (2)

Figure 4 – Lenitudes MC&R's building image (1)

- Imaging – includes echography, radiology and mammography, with special attention for two echo graphs (LOGIQ C5® and LOGIQ E9 XdClear®), one mammography (Senographe Essential®), one ultimate model of echocardiograph (VIVID E9 XdClear®) and the surgery X-Ray arch C (Brivo Essential®), that constitute also cutting-edge devices;
- Radiotherapy – Lenitudes MC&R offers a more precise treatment, since the two Elekta accelerators produce a more accurate radiation beam, in a fewer time, causing less collateral damage. In this way, the healthy cells located near the tumour will hardly be affected;
- Outpatient surgery – the unit has the two surgical rooms equipped with high technology, which will be used by multidisciplinary surgical teams, plus three recovery areas (including four bedrooms). In future, the professionals will use advanced surgical techniques, and even irreversible electroporation procedures;
- Chemotherapy (medical oncology) – with four individual rooms and one larger room for four patients;
- Clinic consultations, including several medical specialties: psychology and nutrition, gynaecology/urology, otorhinolaryngology, neurology, gastroenterology, anaesthesiology and pain, orthopaedic, psychiatry, dermatology, radiotherapy, nuclear medicine, cardiology, pulmonology and medical oncology;
- R&D – within two laboratories, one for basic research and other for clinical research;
- Palliative care and partnerships with other clinical centres.

Although Lenitudes MC&R unit intends to focus on cancer patients, it presents more valences which expand its activity. The nuclear medicine devices can be used for diagnosing other diseases, consulting rooms are intended to multiple medical specialties and it is also possible to perform surgical procedures for other pathologies beyond cancer. This clinic aims to go further, offering sleep studies, clinical trials, neurological research

related to nuclear medicine techniques. The management and clinical evaluation of the results of each treatment will allow the unit to provide a more personalized treatment for each patient. In conclusion, the Lenitudes MC&R is very committed to offer quality services, keeping in mind its continuous improvement, ensuring the satisfaction of the expectations and needs of the patient.

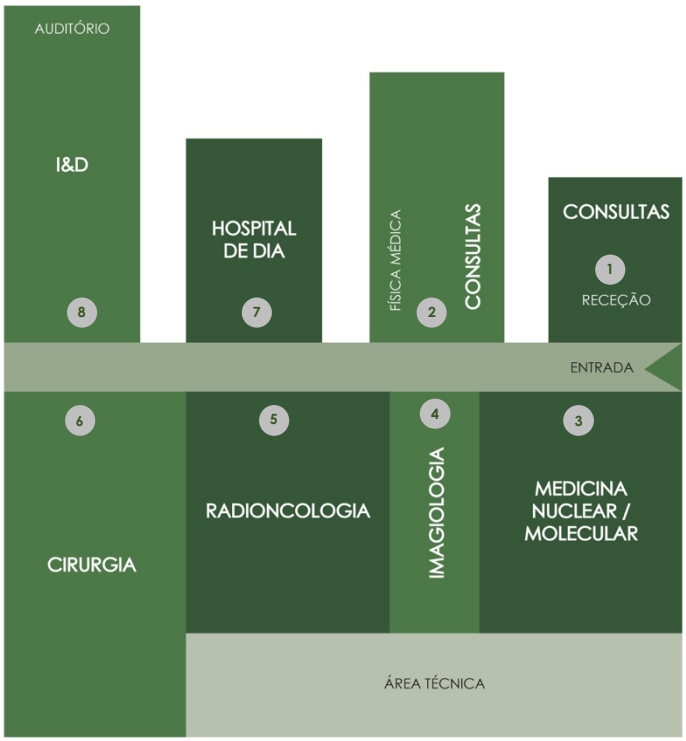


Figure 5 - Lenitudes MC&R's map drawing (1 - Reception, 2 - Consultation/Examination rooms, 3 - Nuclear Medicine and Molecular Imaging, 4 - Imagiology, 5 - Radiotherapy, 6 - Surgery, 7 - Day Hospital, 8 - Administration and Research & Development) (1)

1.3 Reports' Structure

This report is structured in order to, in this section, provide a brief overview of the institution, as well as the proposed objectives for my internship. This chapter is followed by a general framework on safety in health care, the impact of AE and the importance of surveillance and reporting. Then risk management is introduced, identifying the main methods and clarifying its fundamental importance to the company in question.

In the following chapters, the multidisciplinary experience and all the activities that I have participated during this period will be described. A brief discussion and conclusion will be presented at the end, displaying my personal opinion, the main obstacles faced during this period, as well as the skills acquired, learning outcomes achieved and its importance to my personal, interpersonal and professional growth.

2. General Framework

Health facilities have the main mission of providing their patients a range of services with high quality and efficiency, based on the best evidence available, free of damage and risks, ensuring the satisfaction and personal safety of individuals (3). However, as in any other area, there is always a chance of failure and a risk inherent in the professional practice (3,4). Failures resulting from health care have a direct implication on patients and inevitably compromise the main mission defended. Because of the impact caused, either on patient or in health facilities, in the last two decades the subject of security in health care has become a central issue for the scientific community from many countries of Europe and the world, constituting an essential area of health quality (3–5).

According to Conceptual Framework for the International Classification for Patient Safety (ICPS), published in 2009 by the World Health Organization (WHO) and by the Health Direction (Direção-Geral da Saúde – DGS in Portuguese) in 2011, patient safety can be defined as "the reduction of the risk of unnecessary harm associated to health care, to an acceptable minimum"[1] (6). As it is accepted that the risk is a constant in health care, it is also assumed that it is impossible to eliminate it completely, being a minimum level accepted. This level of residual risk is weight taking into account the current knowledge in the area, the resources available and the context in which care is provided, compared to the risk of an alternative treatment or even with the patient's risk of not being subject to no treatment (3,6). Errors are considered failures in carrying out a planned action in accordance with the provisions or the incorrect development of a plan (6). These faults have unintended nature and can manifest through the practice of a wrong action or are unable to perform the correct action, either in its planning or execution (3,6). When a change occurs in a procedure, in a deliberate and intentional way, this deviation is not considered an error, but a violation (6). Both errors and violations increase the risk to the patient and, consequently, added the probability of an incident. According to the ICPS, an incident is usually unexpected and undesirable occurrence, which may have led, or actually led to unintended damage and/or unnecessary for the patient (6). In this same document, the incidents are classified into 13 different types including (6):

1. Clinical administration;
2. Clinical process/procedure;

[1] In portuguese definition: “segurança do doente é a redução do risco de danos desnecessários relacionados com os cuidados de saúde, para um mínimo aceitável”.

3. Documentation;
4. Healthcare associated infection;
5. Medication/intravenous fluids;
6. Blood/blood products;
7. Nutrition;
8. Oxygen/gas/vapour;
9. Medical devices/equipment;
10. Behavior;
11. Patient accidents;
12. Infrastructure/buildings/fixtures;
13. Resources/organizational management.

In addition to its type, depending on the attributes which it presents, an incident can be a reportable circumstance, near miss, no harm incident or harmful incident/AE (Table 1) (6).

Table 1 - Class attributes of patient safety incidents (6)

Reportable circumstance	A situation in which there was significant potential for harm, but no incident occurred.
Almost event *(near miss)*	An incident which did not reach the patient.
No harm incident	An incident which reached a patient but no discernable harm resulted.
Harmful incident (AE)	An incident involving harm to the structure or function of the body and/or any deleterious resulting effect (illness, injury, suffering, disability or death).

The AE represent the class of incidents with greatest concern, since in these situations, damage caused in the course of care, rather than the underlying disease, results in measurable disability for the patient. These incidents are therapeutic adversity, iatrogenic damage or other events caused by complications with drugs, medical devices, infected wounds, complications caused by neglect, misdiagnosis, maladjusted therapies, etc. (6). We are facing an Adverse Drug Event (ADE) when any unfavorable and unintended occurrence happens after using a drug, regardless of the existence of a causal link between the AE and the administration or taking the medication (6–8). This event is only considered

as an Adverse Drug Reaction (ADR) if it is actually proven that the drug was responsible for the unwanted occurrence, that is, whenever there is actually a possible causal link between the occurrence of the AE and the use of the product (figure 6). This includes all situations resulting from the use of a drug according to the marketing authorization as well as those that occur in a use that is not in as described in the Summary of Product Characteristics (SmPC) and the Package Leaflet (PL), including those resulting from medication errors, misuse, abuse or resulting from occupational exposure to drug (6–8).

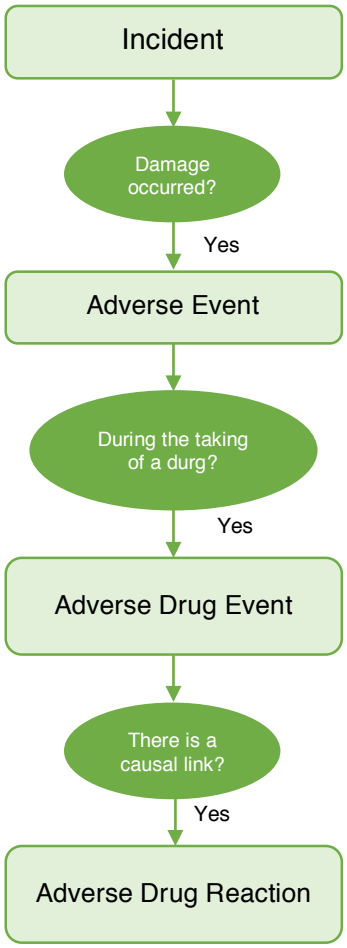


Figure 6 - Representation of the relationship of the terms: incident, AE, ADE and ADR.

When damage occurs to the patient is extremely important to identify the severity and duration, as well as the resulting implications on the treatment of the incident. The degree of damage to the patient as a result of an AE is described in Table 2.

However, it should be noted that, apart from the cost in human lives, the failures in health care may have other negative consequences, namely (3,9):

- Loss of confidence in the health units and their professionals by the users, with consequent deterioration of relations between them;
- Frustration on the part of health professionals for not being able to provide the best possible care;
- Reduced ability to achieve the results planned by health facilities, with direct consequences on the quality of care.
- Increased social and economic costs - increase in days of hospitalization, reduced productivity, suffering and emotional distress for the patient and family.

Table 2 - Degree of damage to the patient (6)

Degree	
None	The consequence in patient is asymptomatic and do not require treatment.
Mild	The consequence in patient is symptomatic, with mild symptoms, loss of functions or intermediate or minimum damage of short duration, without intervention or with minimum intervention required.
Moderate	The consequence in patient is symptomatic, requiring intervention, an increase in the stay, or cause permanent/long term damage, or loss of function.
Serious	The consequence in patient is symptomatic, requiring intervention to save the life, major medical/surgical intervention, shortens life expectancy or cause permanent damage large/long term, or loss of function.
Death	In the balance of probabilities, the death was caused or anticipated in the short term by the incident.

Identify where and when did the mishaps occur during the provision of health care and change processes in order to reduce the possibility of damage, requires reliable data on the occurrence of preventable AE. According to WHO, the insecurity in health care is a serious public health problem, constituting a major cause of morbidity and mortality worldwide (10). Through a meta-analysis involving 39 prospective studies conducted in the United States of America (USA) over a period of 32 years, it was estimated that in 1994 died approximately 106 000 patients hospitalized due to severe ADR constituting the 4th-6th leading cause of death that year (11,12). In the early twenty-first century, the report "To err is human" published by the Institute of Medicine (IOM) has strengthened the concern previously raised. According to results released it was estimated that each year die about 44-98 thousand patients in the USA due to damage resulting from healthcare and not of their

illness, assuming a high mortality rate compared to the values attributed to diseases such as Acquired Immunodeficiency Syndrome (AIDS) and breast cancer (9). Around the same time, also in Europe were beginning to release data on the impact of AE. According to the report "An Organization with a Memory," in the United Kingdom (UK), in 1999, at least 400 patients died or were seriously injured by AE with medical devices and nearly 10 000 people suffered serious ADR. The global estimate is that every year there are about 850 000 AE in the british national health service, which translates into 2 billion pounds in additional hospital day costs (13,14). Alongside these publications, also a spanish study showed that 9.3% of patients in Spain in 2005 suffered AE, of which 42.8% were considered preventable (14). Based on the results of national surveys and interviews, the Commission of the European Communities (CEC) estimates that between 8 and 12% of inpatients in European Union (EU) hospitals are AE victims during their treatment (14).

In the case of Portugal, the impact of failures on patient safety is not fully known because there is not much information available about the topic. However, the recent study "*Segurança do Doente*" held by the national school of public health takes the first steps in research in this area. This study was conducted in three public hospitals in the Lisbon region and was based on the analysis of the information contained in the medical records of a sample of 1669 patients admitted in 2009. According to the results of the study, was recorded a rate of AE incidence of 11.1% (at the 95% confidence interval), where about 53.2% of the cases were considered preventable. As regards to the clinical impact, the presence of damage or permanent dysfunction occurred in 5.7% of cases and 10% mortality occurred. In 58.7% of cases there was prolongation of hospital stay, with an average of 10.7 days (with the respective additional costs) (5). With regard to distribution by age groups, the number of AE varied in proportion of older age (5). In general, the results reported in this study demonstrate that the national picture is not very different from those described in identical studies conducted in other european countries or the United States of America (USA).

Although incidents are harmful in any clinical context, oncology poses particular challenges, as it is full of uncertainties and can be difficult to see if it really was a medical error (15). This becomes even more complicated due to the toxic nature of many of the therapies used in treating cancer and, on the other hand, due to the fact that there is a higher incidence of this disease in the elderly population (15). It is known that elderly patients are more likely to experience AE. This fact can be explained by the higher number of chronic diseases present and taking multiple concomitant medications in a prolonged

form, resulting in a change in the processes of excretion and elimination and the levels of plasma proteins (15). Therefore, despite all precautions, the exposure of the population to cancer chemotherapy is associated with a considerable risk of severe AE for patients, and there is a serious potential for medical errors (16). In 2009 it was published a study by the university of Freiburg medical centre (Germany) which evaluated the quality and safety of cancer treatment, with regard to medical errors associated with chemotherapy and severe AE resulting from this. According to the results released, during the two years of the study there were detected medical and administrative errors in 17.1% of cases of chemotherapy: 3.8% of the errors involved problems in the order of treatment (dose, drug), 4.5% were related to faults in the patient information (height, weight, cycle), while in 8.7% of the errors was missing informed consent signed by the patient (16). Concerning the AE, it is known that anticancer therapies carry a large number of associated complications, such as myelosuppression (leucopenia, neutropenia, thrombocytopenia), infections, nausea, vomiting and diarrhea (17). As these complications are usually related to the properties of the drugs involved, the study mentioned did not focused on them, and tried to identify avoidable serious AE in clinical practice, to attend on them and ensure a safer delivery of care (Table 3) (16). As can be seen by the data in table 3, despite the efforts of health professionals, still occur severe AE that can be effectively avoided or minimized assuming an error monitoring position. Proof that this is possible is that at the end of the study presented, the error rate intercepted by the working group was around 99.9%, with only three serious ADR associated with chemotherapy occurred due to incorrect treatment or orders not intercepted (16).

Table 3 - Classification of severe AE occurred in cancer patients treated with chemotherapy (adapted from (16))

Severe AE	Number of cases	Percentage
Unexpected death	71	40,8%
Transfer to the intensive care unit	66	37,9%
Unexpected operations	5	3,8%
Extravasation of anticancer drugs	12	6,9%
Others	20	11,5%
Total	174	100%

The decrease that occurred in the error rate was achieved through the implementation of efficient surveillance systems, important safety verification tools to ensure that cancer treatments are delivered to patients with fewer errors.

Similar to what happens in chemotherapy, when about two-thirds of cancer patients undergo radiation therapy, adverse reactions may arise (18). Generally, AE begin in the second or third week of treatment and may persist for several weeks after the last session. The EA associated with radiotherapy can be classified as acute – occur during treatment or shortly after its completion and generally disappear within four to six weeks – or late – observed months to years after completion of treatment and often permanent (18,19). As radiotherapy is a localized treatment, the radiation affects only the area of the irradiated body. However, it is common for patients to manifest asthenia, being particularly enhanced if they are receiving other treatments simultaneously (18,19). Most side effects disappear after treatment, although some persist, recur or develop it later. In addition to general side effects, some AE of therapy depend on the type and location of the radiation, as can be seen in table 4.

Table 4 – Acute AE of radiation therapy, by tumor location (adapted from (19))

Location of the tumor \ Adverse effect		Nausea	Diarrhea	Alopecia	Radiodermitis	Odynophagia	Dysphagia	Dysphonia	Xerostomia	Dysgeusia	Mucositis	Cough	Pollakiuria	Dysuria	Nocturia	Cytopenia	Other side effects
Central Nervous System (CNS)	Brain	✓		✓	✓												Headache Earache Brain edema
	Others																
Head and neck				✓	✓	✓	✓	✓	✓	✓	✓						Weight loss
Chest	Breast				✓	✓	✓	✓				✓				✓	Pneumonia Pericarditis Myocarditis
	Lung																
	Others																
Abdomen and pelvis	Urology	✓	✓		✓								✓	✓	✓	✓	Abdominal pain Rectal tenesmus Proctitis Sigmoidite
	Gynecology																
	Colo-Retal																
	Others																
Skin and extremities					✓												Erythema Dermatitis

Taking into account the numerous AE that may arise, it becomes clear that the monitoring of the safety of the treatments is an essential element in the effective use of high-quality medical care. The implementation of effective surveillance systems is critical to

make proper management of toxicity associated with the treatments and to provide a safer and more benefits treatment with less damage to the patient.

Given this panorama, it is essential to identify factors that may contribute to insecurity in health care. A very mentioned problem relates to the decentralized and fragmented nature of care (9). When patients are seen by multiple providers in different contexts, it is not always assured full access to information, making it easier the occurrence of errors or not allowing early detection of AE (9). On the other hand, the absence of general and specific guidelines setting out actions focused on analyzing the causes of the errors, allied to insufficient information, inadequate and difficult to obtain, constitute additional difficulties. Finally, the prevalence of a blame culture towards the failures and consequences, associated with the underutilization of the AE reporting system, stops improvements in this area (3).

Faced with this evidence, both the WHO and the EU have recommended to several countries to assess and monitor the patient safety culture in healthcare units, in order to introduce changes and achieve better safety and quality levels (20). Incidents can be prevented through designing a safer health system, in order to make it easier to perform the action correctly and difficult to do anything wrong. Health organizations should aim to develop a "safety culture" so that all processes are focused on increasing the safety of patient care. One of the most important attributes of organizations with high reliability is a concern on the possibility of failure, admitting that mistakes exist and train professionals to recognize these failures (20).

In Portugal, the recommendations of international organizations were heard and patient safety is now a priority of the national strategy for quality in health 2015-2020, which is part of the national plan for patient safety (20). The first phase of development of safety culture involves the assessment of the current safety culture of healthcare organizations. By standard no. 025/2013 of 24 December was instituted this assessment, settling stages of the process of assessing and monitoring the patient safety culture in the national health system. In August 2015 the report of this study, promoted by DGS and the Portuguese Association for Hospital Development (Associação Portuguesa para o Desenvolvimento Hospitalar – APDH in Portuguese), was published with data from 55 hospitals in the year 2014. In this first national assessment, it can be concluded that the patient safety culture is not yet widely accepted as a priority by professionals and institutions. About 63% of the respondents described not having made any incident report in the last 12 months, a

significant proportion feels that mistakes are used against them and the notifier is the focus of attention and not the problem itself (20).

Knowledge and understanding of the incident, as the frequency, causes and impact, are a key part of the process of assessment and continuous improvement of patient safety and healthcare quality (21). Pharmacovigilance plays an essential role in the early detection of risks of medicines. Each drug is tested on a relatively small proportion of the population before it is approved for use by the general population, where the ADR that have not been previously detected can arise. Thus, pharmacovigilance plays a key role in benefit/risk assessment and the criteria and methods for therapeutic use (21,22). At the national level, since 1992 there is the National Pharmacovigilance System (Sistema Nacional de Farmacovigilância – SNF in Portuguese) that is capable of monitoring the safety of medicines. The role of the SNF is to detect, collect, evaluate and understand information about ADR and to establish the responsibilities of the marketing authorizations holders of medicinal products, health professionals and health authorities (11,22). The establishment of such systems is particularly relevant in terms of public health protection of citizens and requires appropriate involvement of all stakeholders (11). The surveillance of medicinal products focuses mainly on spontaneous reporting of ADR and suspected severe ADR performed by health professionals and users to the regional unit of pharmacovigilance or to Infarmed, by completing an online form, paper or by phone (22). Although one of the major problems identified for the SNF is high underreporting rate, 2012 data show that the spontaneous reporting ADR has evolved positively, quite close to the value of 200 reports/million inhabitants recommended by WHO, placing the country in a favorable position regarding this issue (22). In the national context, all reports of suspected ADR are evaluated, it is allocated to each a degree of probability and a causality assessment is accomplished through the global introspection method or clinical diagnosis (22). With regard to its participation as a member of the Risk Management Committee on Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA), Infarmed put Portugal in 2015, in the 3rd position in european system of evaluation as pharmacovigilance rapporteur (responsible for monitoring and evaluation of medicinal products in Europe) (23). With regard to Medical Devices (MD) it is up to National Authority of Medicines and Health Products, I.P. (Autoridade Nacional do Medicamento e Produtos de Saúde – INFARMED in Portuguese) to ensure the supervision of them and maintenance of the National Surveillance System of MD. This system aims to minimize the risks of the use of MD and ensure the implementation of preventive and corrective measures,

encouraging the reporting of incidents with MD (24). There must be notified through appropriate forms available, all suspected of a serious event related to the MD – life threatening situations that put life at risk, cause disability or permanent injury, hospitalization or prolongation of that, which causes suffering, anomaly or fetal death (24).

Alongside these two systems, at the end of 2012 the DGS also made available to health professionals and citizens, the National System of Incidents – NOTIFICA. This system is structured in accordance with the recommendations of WHO (adopting the 13 kinds of incidents defined in the ICPS) and intends that the errors to be reported confidentially, either by health professionals or by citizens, so that they can be examined individually and that teams can learn from the error (25,26). It is characterized for being an online, anonymous and non-punitive platform, which allows the management of incidents and AE, occurring at all levels and areas of healthcare units of the health system. According to the 3rd quarter of 2015 monitoring progress report, the most reported incidents, either by professionals or citizens, are relate to clinical procedures, administrative and infections (27).

The occurrence of preventable Serious Adverse Event (SAE) in health care suggests, although it does not prove, that there is a failure in the health organization efforts to safeguard patient safety. Therefore, AE reporting systems are seen as an invaluable warning systems, and are strongly recommended in all institutions who undergo external accreditation processes, either through the Joint Commission on Accreditation of Healthcare Organisations (JCAHO) or Caspe Healthcare Knowledge Systems (CHKS) (11,28,29). With regard to pharmacovigilance, the role of the notification system is irreplaceable, with proven efficacy and a good track record with respect to preventing potential problems and identifying new or unknown AE (11,12).

Given this background, it is easy to see that the AE are clearly important for health organizations, not only because of its impact on patients, but also because they can provide insight into the quality of health care and promote improvement in performance (9). It is consequently crucial that patient safety, reporting and resolution of AE, rather than a necessity, should fall in routine care. It is imminent to implement changes to promote a risk management culture and make all activities safely to patients, reducing the risk of AE (9).

2.1 Regulatory Framework

In order to reduce the number of AE, by collecting better safety data on clinical medicine and procedures, there have been many efforts to make legislation in this area most complete as possible. In 2005, the European Commission initiated a review of the european system of security monitoring, which resulted in the adoption of the new directive and the regulation in December 2010, causing the biggest change in the regulation of human medicines in the EU since 1995 (30). Therefore, in this report were consulted some documents of the current european and national legislation pharmacovigilance, which apply to providers of healthcare units and its professionals:

- Directive 2010/84/EU of 15 December – amending Directive 2001/83/EC in order to strengthen EU law in pharmacovigilance;
- Decree-Law nr. 128/2013 of 5 of September, which is the 8th alteration to the Decree Law nr. 176/2006.

In addition to legislation, there is a guideline with procedures designed to facilitate the performance of pharmacovigilance in the EU – the Good Pharmacovigilance Practice (GVP). Of its various modules, those that have had the most interest for this project were the module V – risk management systems and module VI – management and reporting of adverse reactions to medicinal products. For the analysis of AE and incidents, it was also used the orientation nr. 011/2012 of the DGS.

With regard to risk management, despite not having legal requirements, there has been consulted some documents, which are used as a reference for the implementation of risk management systems in institutions, such as the ISO 31000 and the International Conference on Harmonisation (ICH) Guideline Quality Risk Management - Q9.

2.2 Risk Management

All activities of an organization involve risk, which is commonly defined as the combination of the probability of occurrence of harm and the severity of that damage (31). When it comes to health care, risk management includes all clinical and administrative activities undertaken to identify, assess and reduce the risk of injury to patients, staff and visitors and the risk of loss to the organization itself (32). The risk is inherent in everything the organization does, from treating patients to determine the priorities of care. Therefore, risk management depends on knowledge of how all the components of the system interact with each other. Organizations manage risk by identifying it, analyzing it and then evaluating whether the risk is acceptable or should be reduced. Thus, along with a structured training program for all health unit staff, it can set four main pillars that are the foundation for the operation of a risk management program (33):

1. Incident Reporting System (IRS);
2. Identification and assessment of risk;
3. Monitoring of the patient safety indicators;
4. Audit as continuous improvement instrument.

2.2.1 IRS

The main purpose of an IRS is generating signals that lead to the early identification of potential problems (33). In this way, I intend to analyze the contributing factors, with a view to establishing a plan for improvement in order to prevent their recurrence (11,29,33). The success or failure of any IRS depends on the active participation of reporters. In most cases, the shame and the fear of punishment by professionals, lack of utility perception (especially if there is no adequate feedback) and the difficulty in understanding what constitutes an incident, contribute to the great limitation of these systems: underreporting (11,22,29,33,34). Thus, it is essential to increase the knowledge of the healthcare team about patient safety through training, to instruct the understanding of the different types of incidents, their causes and consequences(22).

In each reported incident, is critical to determine whether it reached or not the patient, if required a new therapeutic intervention, if prolonged hospital stay and caused some damage (29). If done in a systematic manner, this research allows us to determine the priority areas of intervention, either by greater frequency or the more serious the damage

caused (29). Effective implementation of an IRS in a healthcare facility is a slow process that to function properly, needs to (3):

- Develop a culture of responsibility and not punishment;
- Analyze incidents with focus on the system rather than the individual;
- Facilitate communication of AE and allow feedback to stimulate the improvement, preventing new risk events;
- Simplifying the act of notification: few items, but fundamental.

In short, table 5 lists the characteristics that have been identified by several authors as pillars for a successful notification system.

Table 5 - Characteristics of a successful incident reporting system (adapted from (35))

Not punitive	Notifiers are free of fear of retaliation or punishment of others, as a result of the notification.
Confidential	Patient and notifier identities are never revealed to a third party.
Independent	The program is independent of any institution with the power to punish the notifier or organization.
Analyzed by experts	The reports are evaluated by experts who understand the clinical circumstances and are trained to recognize the underlying causes.
Timely	The reports are reviewed promptly and the recommendations are quickly disseminated to the appropriate involved.
Oriented systems	The recommendations focus on changes in the systems, processes or products, rather than on individual performance.
Responsive	The group that analyzes the incidents are able to disseminate the recommendations and answer any questions that may arise during the implementation of the measures proposed process.

Since this is a reactive approach, which is made after the occurrence of a failure, for the analysis of an incident it is necessary to have in mind that an incident is associated with a chain of underlying events, with several factors which have contributed to their occurrence. Therefore, the analysis should be based on the identification of these factors and one of the measures that can be used is the Root Cause Analisys (RCA), shown in figure 7. According with the ICPS, RCA is an iterative systematic process whereby the factors that contribute to an incident are identified, to reconstruct the sequence of events, repeating the question "why" until the underlying root causes are clarified (6).

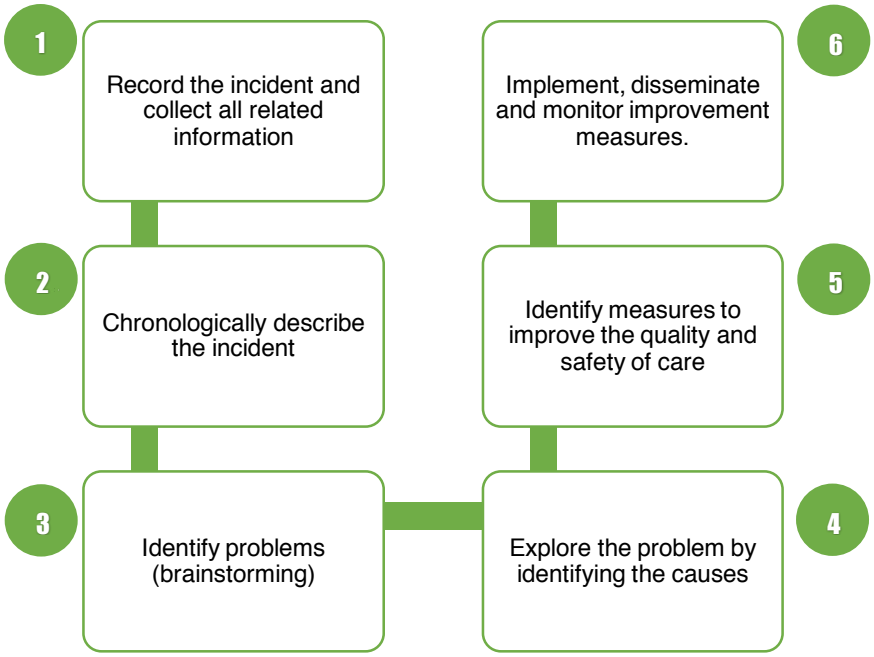


Figure 7 – Steps of RCA (adapted from (33))

The steps followed in the RCA are (36):

- Description of the event: Using medical records, the AE and activities leading up to it must be described in detail. Must be done the record of the incident, specifying the injury or potential injury to the patient. It is important to chronologically describe the incidente through questions such as “when did it occur?” or “what service areas were affected?”;
- Identification of the Proximate Cause(s) (PC) that led to the event: The PC explains why the event occurred. For example, an ADR (the event) occurred because the physician made a request for the wrong antibiotic (PC) that the pharmacy dispensed (PC) and a nurse administered (PC). These PC of AE are flaws in the healthcare process, consequently leading to errors. It may be useful to build an event diagram, showing the steps in the process that failed.
- Identification of the Contributing Factors (CF) that led to the PC: CF permit errors to occur. For example, a nurse who forgot to administer a dose of medication may have been required to do a double shift. Thus, fatigue and staff shortages were the CF to this medication error. CF to AE often fit into the following categories: human resource issues, information availability, environmental issues, culture and communication among clinicians.

- Identify measures to improve the quality and safety of care and implement, disseminate and monitor these measures.

Regarding the AE with drugs, whenever there is a suspicion of an ADR, or an incident with a MD, it is the obligation of the health institution to notify the INFARMED or regional pharmacovigilance units, by appropriate forms available.

2.2.2 Identification and assessment of risk

The methods of identification and risk assessment are a proactive approach that is intended to realize if our activity potentiates adverse and unexpected events, in order to create preventive mechanisms and avoid that these AE occur (figure 8) (33). The organization should define the criteria to be used to assess the significance of the risk, reflecting the values, objectives and organization of resources. It is appropriate that the factors to be considered include aspects such as (37):

- Nature and types of causes and consequences that can occur and how they will be measured;
- How probability is going to be defined;
- Evolution in the probability of the time and/or consequences;
- Risk level to be determined;
- The level at which the risk is acceptable.

1. **Risk assessment** consists on the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazard. Quality risk assessments begin with a well-defined problem description or risk question (31,37).
    - **Risk identification** is an organized use of information to identify hazards referring to the risk question or problem description. The organization should identify sources of risk, causes and potential consequences. Information can include historical data, theoretical analysis, informed opinions, and the concerns of stakeholders. The identification of risks addresses the question "What might go wrong?" (31,37).
    - **Risk analysis** involves understanding the risks, namely the estimate of the risk associated with the identified hazards. It is the process of linking the probability of occurrence and severity of damage. The risk analysis may be performed with various levels of detail depending on the risk involved, the purpose of the

analysis and information available. Depending on the circumstances, the analysis can be qualitative, semi-quantitative or quantitative, or a combination thereof (31,33,37). With qualitative methods it is possible to make a subjective assessment of the activities/processes. It is not intended to quantify the consequence and probability, these assume a purely qualitative dimension (33,36). The semi-quantitative evaluation method associates a numerical value to the probability and consequences identified. In the quantitative method there are used sophisticated techniques and mathematical models that take into account the standards of regularity and frequency of the event, to calculate the probability values. For its complexity this method is used at very high risk areas, such as chemical or nuclear industries (33,36).

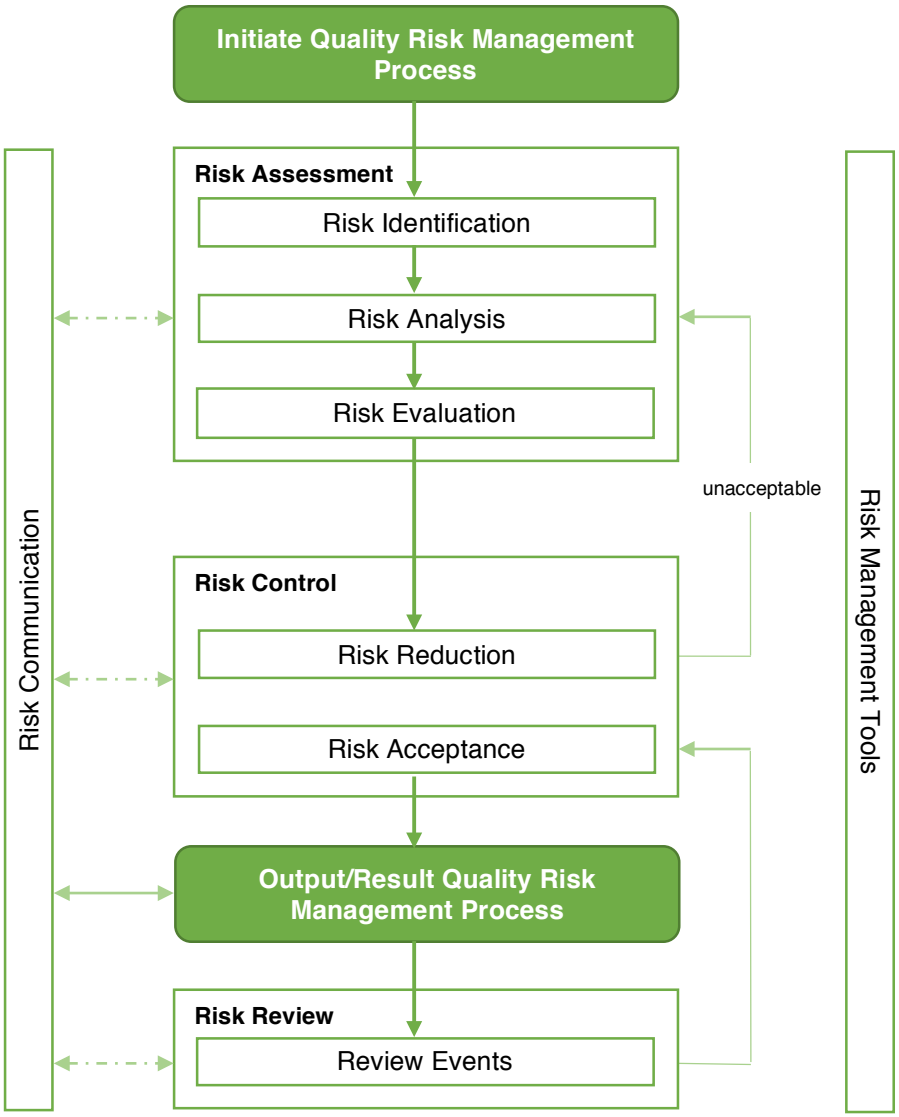


Figure 8 - Overview of a typical quality risk management process (adapted from (31))

Despite the inherent subjectivity, the qualitative method has the advantage of being simple, requiring advanced mathematical knowledge. The table 6 shows the levels of risk classification resulting from the semi-quantitative assessment of the consequence and probability of risk detected, recommended by the National Patient Safety Agency (NPSA) (33,36,38).

- **Risk evaluation** compares the risks identified and analyzed according to established risk criteria. The purpose of evaluation is to help in making decisions based on the results of the risk analysis on which risks need treatment and the priority to the implementation of treatment. When making an assessment of the effective risk, the robustness of the data set is important because it determines the output quality. The output of a risk assessment is either a quantitative or qualitative estimate of risks (31,37).

Table 6 - Risk matrix recommended by NPSA (adapted from (38))

Consequences	Likelihood				
	1	2	3	4	5
	Rare	Unlikely	Possible	Likely	Almost certain
5 Catastrophic	5	10	15	20	25
4 Major	4	8	12	16	20
3 Moderate	3	6	9	12	15
2 Minor	2	4	6	8	10
1 Negligible	1	2	3	4	5

1 - 3	Low risk
4 - 6	Moderate risk
8 - 12	High risk
15-25	Extreme risk

2. **Risk control** involves decisions to reduce to an acceptable level and/or to accept risks. The treatment of risk involves selecting options to modify the risks and the implementation of these options. The amount of effort used for risk control should be proportional to the implication of the risk. Decision makers might use different procedures, including benefit-cost analysis, for understanding the ideal level of risk control (31,37).

- **Risk reduction** includes the actions taken to lessen the probability of occurrence of harm and severity of that harm (31). This focuses on processes for mitigation or prevention of risk (through improving the detection of dangers) when it exceeds a specified acceptable level. Treatment of risks, itself, can introduce risks. Thus, monitoring needs to be part of the risk reduction plan to ensure that the measures remain effective (31,37).
- **Risk acceptance** can be a formal decision to accept the residual risk or it can be a passive decision in which residual risks are not identified (31). For some types of problems, even the best risk management practices might not entirely eliminate the risk and a strategy to accept and manage the risk might be applied (31,37).

3. **Risk communication** is the sharing of information about risk and risk management between the decision makers and others (31). All interested parties can communicate at any stage of the risk management process. It is appropriate that the plans for communication and consultation are developed at an early stage and address issues related to the risk itself, such its nature, probability, severity, control, treatment or other aspects related (31,37).

4. **Risk review** should be an ongoing part of the quality management process, and involve periodic checks or regular surveillance (31). A mechanism to review or monitor events should be implemented to ensure that controls are effective and efficient, information to improve the risk assessment process, analyze the events and identify emerging risks (31,37).

The process of identification and analysis of risk, regardless of the method used, will allow to distinguish between the identified risks, the most serious which therefore require a priority intervention. Risk analysis with techniques such as Failure Mode Effects Analysis (FMEA), Preliminary Hazard Analysis (PHA) or Hazard Operability Analysis (HazOP) allow close scrutiny of the processes but require higher availability and training of the team (31,33). The objective of FMEA is to identify the critical points of processes, evaluate the failures that may occur and their weighting in terms of frequency, severity and risk (31). Once failure modes are established, risk reduction can be used to eliminate, reduce or control the potential failures. This approach is intended to act in the prevention, with a

proactive attitude, complemented by an ongoing notification by the IRS (31,39). It is a powerful tool for summarizing the important modes of failure, factors causing these failures and the likely effects of these failures. For its part, PHA is an analysis tool based on the application of experience or knowledge of a hazard to identify future risks, situations and hazardous events that can cause damage, as well as to estimate the probability of a particular activity. The tool consists of: 1) identifying the possibilities that the risk event happens, 2) qualitative evaluation of the extent of possible injury or damage to health that may result, and 3) a relative hazard classification using a combination of severity and likelihood of occurrence, and 4) the identification of possible corrective measures (31). HazOP is based on a theory that assumes that risk events are caused by deviations from the effective intention. It is a brainstorming technique for identifying hazards using so-called "guide-words". Words such as "no", "more", "beyond" or "part of" are applied to the relevant parameters (e.g., contamination, temperature) to help identify potential deviations from normal (31).

2.2.3 Monitoring of the patient safety indicators

Indicators are a basic tool for health unit management which are used to help to describe the current situation of a particular problem, make comparisons, verify changes or tendencies (39). They permit to evaluate the implementation of the planned actions over a period of time, in terms of quality and quantity of executed health actions (39). An indicator can be a rate or ratio, an absolute number or a fact which can be used as a guide to monitor and evaluate the quality of care provided to the patient (40).

2.2.4 Audit as continuous improvement instrument

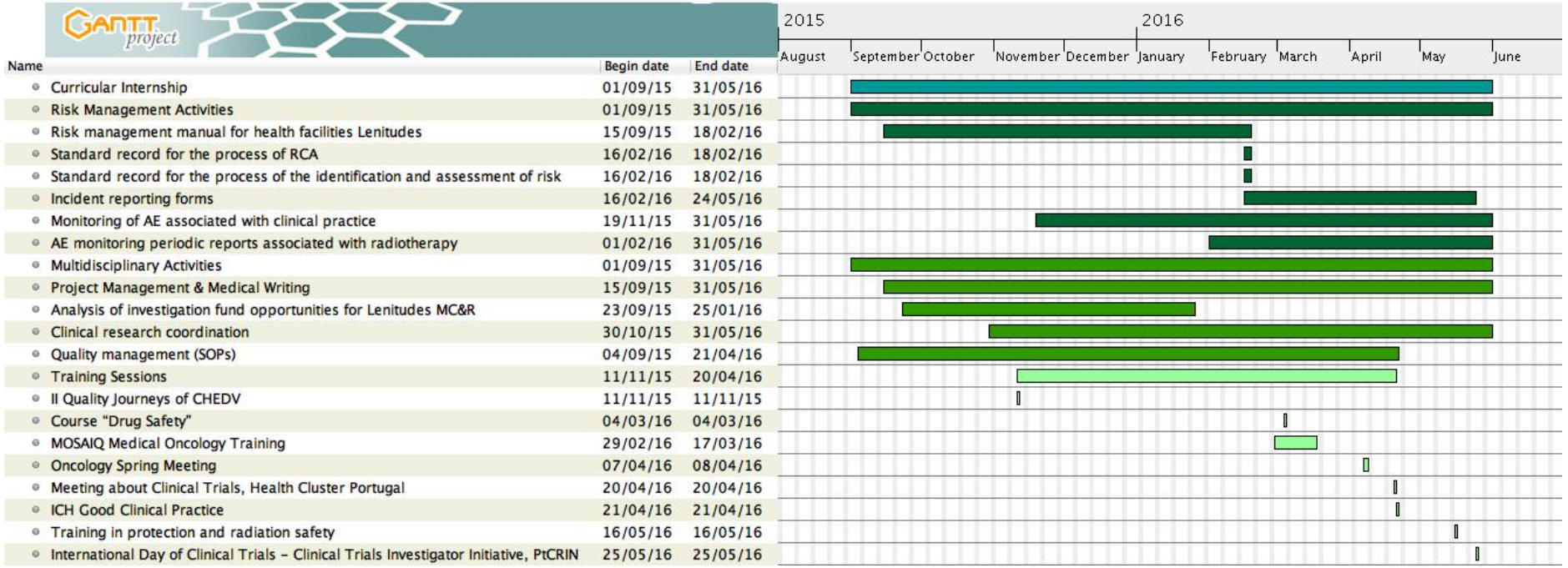
Audit should be seen as an activity for improving both the quality and safety of health care (41). The aspects of performance that are being audited may vary, depending on the interests of those in charge of the audit, and the available information. An audit may, for instance, deal with prescriptions for specific health problems, test ordering, or compliance with disease-specific clinical guidelines. On the other hand, an audit can be based on routinely available data from electronic patient records or medical registries, or on data that are collected by the health professionals specifically for that purpose (41). To establish the frequency and scope of audits, there should be taken into account the existing legal requirements, the robustness of a company's quality risk management activities and the results of previous audits/inspections (31).

3. Activities developed during internship

This chapter intends to describe all the activities, tasks developed and learning outcomes acquired during my curricular internship of nine months at Lenitudes MC&R.

The main functions performed during the internship were activities related to risk management, including the development of the risk management manual, the elaboration of procedures for AE collection and preparation of periodic monitoring reports. Additionally, I had the opportunity to be in contact with different areas, allowing me to performed multidisciplinary activities. Some of this activities encompassed tasks related to R&D, such collaboration as medical writer, project management and collaboration on resarch meetings.

The schedule and duration of the activities are identified in the Gantt chart presented in figure 9. In the following sections are presented the activities that were developed, related to risk management activities and to multidisciplinary activities.



Name	Begin date	End date
Curricular Internship	01/09/15	31/05/16
Risk Management Activities	01/09/15	31/05/16
Risk management manual for health facilities Lenitudes	15/09/15	18/02/16
Standard record for the process of RCA	16/02/16	18/02/16
Standard record for the process of the identification and assessment of risk	16/02/16	18/02/16
Incident reporting forms	16/02/16	24/05/16
Monitoring of AE associated with clinical practice	19/11/15	31/05/16
AE monitoring periodic reports associated with radiotherapy	01/02/16	31/05/16
Multidisciplinary Activities	01/09/15	31/05/16
Project Management & Medical Writing	15/09/15	31/05/16
Analysis of investigation fund opportunities for Lenitudes MC&R	23/09/15	25/01/16
Clinical research coordination	30/10/15	31/05/16
Quality management (SOPs)	04/09/15	21/04/16
Training Sessions	11/11/15	20/04/16
II Quality Journeys of CHEDV	11/11/15	11/11/15
Course "Drug Safety"	04/03/16	04/03/16
MOSAIQ Medical Oncology Training	29/02/16	17/03/16
Oncology Spring Meeting	07/04/16	08/04/16
Meeting about Clinical Trials, Health Cluster Portugal	20/04/16	20/04/16
ICH Good Clinical Practice	21/04/16	21/04/16
Training in protection and radiation safety	16/05/16	16/05/16
International Day of Clinical Trials – Clinical Trials Investigator Initiative, PtCRIN	25/05/16	25/05/16

Figure 9 - Timechart of activities and training sessions developed during the internship.

3.1 Risk Management Activities

As mentioned earlier, my internship began on 1st September of 2015. By this time, the Lenitudes MC&R was in the early phase of its activity, going through the licensing process for the various activities: surgery, radiotherapy and nuclear medicine. Despite R&D is being part of the objectives to be followed in this health unit, at this early stage, it was not possible to develop only tasks inserted in this context. Thus, in the first meeting before the internship started, it was proposed that it was developed in another equally important area for health unit – Risk management and Pharmacovigilance.

In order to be prepared to carry out activities related to risk management it was necessary to carry out an extensive research and review of the available literature. To read and understand the international standards, the guidelines of the authorities and do some training courses were essential to develop the tasks mentioned in the following chapters.

The risk management activities included the development of the following documents:

1. Risk management manual for health facilities Lenitudes;
2. Standard record for the process of RCA;
3. Standard record for the process of the identification and assessment of risk;
4. Incident reporting forms;
5. Monitoring of AE associated with clinical practice;
6. AE monitoring periodic reports associated with radiotherapy.

All documents have been developed in a simple way in order to ensure that they are easily understood by all staff involved.

3.1.1 Risk management manual for health facilities Lenitudes

Keeping in mind the importance that risk management has for health facilities providing health care of high quality and safety, came the opportunity to take the first steps in this area in the development of Lenitudes. So, I proposed and developed an early version of "Risk management manual" in order to begin to set the strategy to be adopted by health units Lenitudes (see annex I).

According to the rules previously established by documentation control SOP developed by the quality system of the unit, the manual has been drafted and is organized into the following chapters:

1. Summary;
2. Introduction – includes a brief description of the structure and organization chart of Lenitudes, and shows the importance of risk management for the unit;
3. Purpose – presents the main objectives of creating this policy:
    - To prevent, manage, analyze, minimize, implement actions related to clinical risk and non-clinical;
    - To maximizing the quality of care by reducing the risk to an acceptable level;
    - To provide the effectiveness and efficiency of risk management;
    - To promote the systematic analysis of risk management performance through indicators and audits;
    - To minimize the costs of risks (human and financial);
4. Mission – describes the mission of the risk management system;
5. Organization and Responsibilities – describes the major responsibilities of the administrative board, the technical support group risk management and other groups;
6. Risk Management – overview system and its four pillars, shown in Figure 10:
    - IRS;
    - Identification and assessment of risk;
    - Monitoring of the patient safety indicators;
    - Audit as continuous improvement instrument;
7. Hospital emergency plan;
8. Policy for sharing information;
9. Record of document revisions.

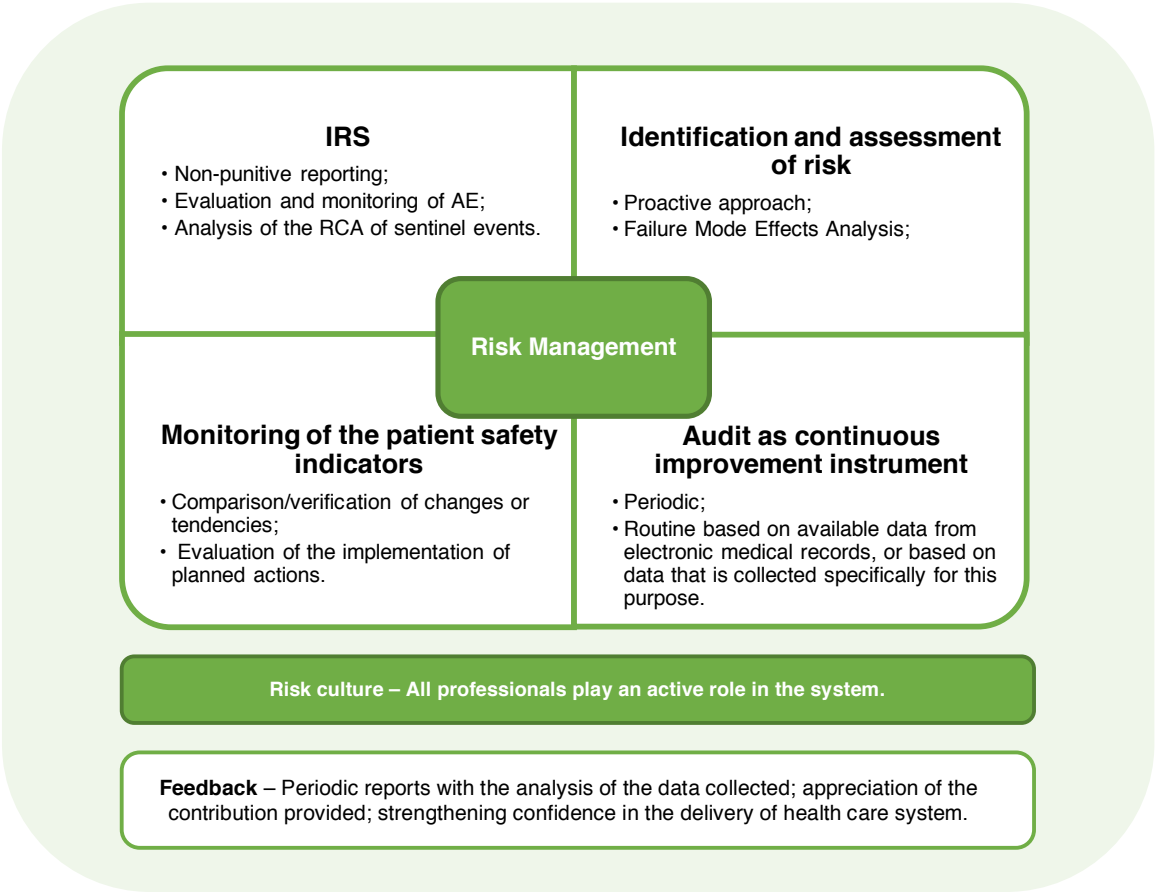


Figure 10 - Representative scheme of the Risk Management System (scheme designed by the author).

In the section six of the manual are given some suggestions on the methods to be adopted taking into account the structure and reality of health facilities of Lenitudes. The strategy presented was developed by me and reviewed by Prof. Francisco Pimentel.

With regard to the reactive approach, it is suggested that the RCA team is composed by a coordinator of the team, a senior professional, one or two professionals with specific knowledge in the area, possibly one or more specialized consultants and a top manager of the organization. As the activities associated with RCA constitute a complex process that involves a cost which can be significant, it is recommended that not all incidents are subjected to this analysis. The decision to perform or not the RCA depends on the severity of the incident, its frequency, the contributing factors and likelihood to happen again. The JCAHO only requires its implementation in sentinel events, and therefore, it is recommended that Lenitudes follows this recommendation. In this regard it should be consulted the 'decision tree of incidents' to help determine whether or not to perform an RCA. The decision must be made before the work of the RCA team starts. In the manual is also established that, in the case of Lenitudes MC&R, the incident notification should be

made by the record of the occurrence in the "Risk Management Platform" (initially, this platform is composed of forms in paper format). Thus, whenever there is a suspicion of an ADR, an incident with a medical device, or a problem in a procedure, it shall be recorded in accordance with the respective internal procedures of the institution.

Regarding the proactive approach, in the manual it is suggested to adopt a method of semi-quantitative risk analysis as recommended by the NPSA, due to its easy use and interpretation. It is also presented the algorithm for identification and risk assessment designed to guide the implementation of this process.

With regard to patient safety indicators, taking into account the health unit characteristics, the following indicators were defined to be monitored in order to reflect the safety of care:

- Rate of return to the operating room unplanned;
- Infection rate of surgical wound;
- Reintervention rate up to 30 days of post-operative;
- Mortality rate up to 30 days of post-operative;
- Infection rate of operated patients;
- AE rate associated with ambulatory surgery;
- Rate of haemorrhage/haematoma postoperative annually;
- Number of reported AE associated with medication;
- AE rate associated with transfusions.

This document should be reviewed at least once a year. However, considering the development phase of Lenitudes, it should be updated whenever new information arise and is approved.

3.1.2 Standard record for the process of RCA

This standard record was written by me under the reactive approach – namely the RCA – presented in the risk management manual. If a particular incident that occurred with significant gravity during clinical practice in Lenitudes is notified, it is advisable to investigate the causes and contributing factors that provided the occurrence of the incident. This process requires a lot of retrospective analysis, check in detail what has been done and it is essential to document all the steps covered. Thus, and according to orientation number 011/2012 of the DGS, a standard record was created in order to keep documentation organized, tracked, and updated. This summary should contain the main topics of the RCA,

such as a brief description of the incident/clinical event, date and time of the incident, notifier name and service in he/she which performs functions, the proximate causes, contributing factors and recommendations for possible measures to be taken to prevent the recurrence of the incident (see annex II). The responsibility of writing this record is of members of the RCA team.

In addition to this record, at the end of the process, should be attached the following documents with greater detail on the RCA process:

- Flowchart with the sequence of events – at the end should be possible to define what happened, with whom, when, where, why, how it happened and, if possible, the increased cost associated with the incident;
- Flowchart from the sequence of expected or defined procedures in accordance with the rules established in the institution;
- Improvement actions list, implemented immediately after the incident;
- Literature review related to the nature of the incident under investigation;
- List and description of existing barriers;
- List of CF obtained through brainstorming, which may have been crucial for the development of the incident;
- List of improvement plans including indicators, temporal goals and objective measures;
- Results report.

This document should be reviewed at least once a year, if there is no indication on the contrary.

3.1.3 Standard record for the process of the identification and assessment of risk

In order to proceed taking into account the recommendations described in the risk management manual, this record was developed under the proactive approach to risk management. Contrary to the RCA which is developed after an incident has taken place, trying to identify the causes to minimize recurrences, the proactive approach aims to identify and assess the risk before the incident occurs. One of the techniques recommended in the manual is FMEA approach. This technique attempts to identify, for a specific process, the critical points, the failures that can occur and their weight in terms of frequency, severity and risk.

Once the potential methods of failure are identified, risk reduction measures can be applied to eliminate or control the risk. Therefore, if a situation in clinical practice justifies initiating this process, it is crucial to document the information gathered in all these steps, in an objective way and following the quality standards. In this sense, I drafted the standard record in question, including the following fields that summarize the main topics of this approach (see annex III):

- Date;
- Name of the procedure/medical device;
- Risk class equipment (if applicable);
- Hazards/risks identified;
- Risk assigned by a semi-quantitative assessment (consequnce x probability);
- Risk control measures.

The completion of this record is the responsibility of the members of the risk management team that perform the procedures for risk analysis and identification.

This document should be reviewed at least once a year, if there is no indication on the contrary.

3.1.4 Incident reporting forms

3.1.4.1 For MD

When I started my internship at Lenitudes MC&R had already been produced some documents in the context of risk management. One of this documents was a form for recording radiological events, prepared by the radiation therapy team. In this document it is recorded the place of occurrence, the person who identified the class of occurrence (near miss, incident without damage, AE, sentinel event), consequences and preventive measures. However, it was missing develop a notification form for incidents in an important area: MD. Thus, based on the topics present in the MD incident notification form of INFARMED, and existing internal SOP for reporting incidents, I drew up a form for the registration of these incidents. This incident reporting form is important to compile information relating to incidents in a systematic and uniform manner to all cases. This form contains the following fields:

- Notifier – name, profession, e-mail, date of notification, signature;
- Suspected MD – commercial name, model, serial number or batch, manufacturer, distributor;

- Information about the patient – identification (name initials), date of birth, sex;
- Incident – date and place where the incident occurred, description, consequences for the patient, evolution of the patient (at the time of notification), similar events;
- Additional comments.

Any health care professional who, due to the clinical activity, encounter an incident with an MD, must notify the case to the risk management team by completing this form. This document should be reviewed at least once a year, if there is no indication on the contrary.

3.1.4.2 For drugs

Apart form for reporting incidents involving MD was also necessary to draw up a form focused to the ADR notification. Once the clinical activity was initiated in Lenitudes MC&R, it became necessary to create a support for the characterization of ADR which occur during the course of treatment or diagnostic tests using drugs (eg. cardiac stress test by chemical stress). In this sense, I developed a form adapted to the reality of the clinic which contains the following fields (see annex IV):

- Patient information (process number, name, date of birth, age, sex, weight and height);
- Characterisation of ADR (start and end date, description, severity and outcome);
- Information about the suspected drug (dose, frequency, route of administration, lot, expiry date, start and end date and therapeutic indication);
- Information about concomitant medication (dose, frequency, route of administration, lot, expiry date, start and end date and therapeutic indication);
- Other relevant information (similar history of ADR, allergies, pregnancy, re-exposure to the drug);
- Management of ADR (drug therapy support, patient hospitalization, classification of ADR);
- Information about the notifier (name, profession, personnel number, e-mail, signature and date).

This document presents with a similar format to the forms of spontaneous reporting provided by INFARMED, integrating the required fields to register the case and forward it to the responsible authority. This document should be reviewed at least once a year, if there is no indication on the contrary.

3.1.5 Monitoring of AE associated with clinical practice

The development of a positive clinical outcome depends, among other factors, of an adequate management of the toxicity of treatments provided. When this fact is not taken into account, the AE associated with treatments often cause morbidity for patients. In this sense, the monitoring of the safety of treatments, especially anticancer therapies whose toxicity is considerably high, it is essential for a high-quality medical care (16).

It was in this context that in the first phase of my internship, it was proposed to develop an AE reporting system in chemotherapy. This reactive approach, where the problem analysis is made after notification, aims to evaluate the toxicity of the different therapeutic regimens. The Lenitudes MC&R wanted the notification of AE to occur in an integrated manner in the clinical record system. To this end, it was necessary to previously input into the computer system a database with the main AE associated with each chemotherapy regimens used.

In this sense, I started to define some of the most frequent therapeutic regimens for each of the most common cancers, with the help of the medical director and the pharmaceutical responsible. After that, I collected information in the medical literature about the toxicity associated with these treatments, and defined the percentage theoretically expected for the occurrence of each AE. The example below shows the result of this exercise performed for three of the most common regimens in breast cancer therapy, colorectal and lung cancer – FEC, FOLFOX 6 and Pemetrexed+Cisplatin, respectively (tables 7,8 and 9).

Table 7 – Most frequent AE of FEC regimen for the treatment of breast cancer (adapted from (42))

	Leukopenia/ Neutropenia Grade 3-4 Toxicity	Anemia Toxicity		Other Grade 3-4 Toxicities		Emetogenic potential	Selected Consequences of AEs
FEC 100 N=276	Neutropenia 25%	Grade 1-2	42%	Infection (Grade 3)	3%	Day 1 – level 5	4 cases of delayed cardiac toxicity
				Stomatitis	4%		
		Grade 3	1%	Alopecia	79%		
				Nausea/Vomiting	35%		

Table 8 - Most frequent AE of FOLFOX 6 regimen for the treatment of colorectal cancer (adapted from (42))

	Leukopenia/ Neutropenia Grade 3-4 Toxicity		Anemia Toxicity		Other Grade 3-4 Toxicities		Emetogenic potential	Selected Consequences of AEs
FOLFOX 6 <u>First line</u> N=110 <u>Second line</u> N=82	*First line*		*First line*		*First line*		Day 1 – level 4 Day 2 – level 2	1 therapy-related death with FOLFOX when used as first line 11% of patients discontinued therapy due to toxicity
	Neutropenia Grade 3	31%	Grade 1	39%	Thrombocytopenia (Grade 3)	5%		
					Mucositis (Grade 3)	1%		
	Neutropenia Grade 4	13%	Grade 2	12%	Neurological (Grade 3)	34%		
					Diarrhea	11%		
					Fatigue (Grade 3)	3%		
			Grade 3	3%	Nausea (Grade 3)	3%		
					Vomiting (Grade 3)	3%		
	Second line		*Second line*		*Second line*			
	Neutropenia Grade 3	15%	Grade 1	35%	Thrombocytopenia (Grade 4)	1%		
	Neutropenia Grade 4	2%	Grade 2	9%	Mucositis (Grade 3)	4%		
					Neurological (Grade 3)	20%		
					Nausea (Grade 3)	6%		
			Grade 3	2%	Diarrhea	5%		
					Fatigue (Grade 3)	5%		
			Grade 4	1%	Vomiting (Grade 3)	5%		

Table 9 - Most frequent AE of Pemetrexed + Cisplatin regimen for the treatment of Non-small Cell Lung Cancer (adapted from (43))

	Leukopenia/ Neutropenia Grade 3-4 Toxicity		Anemia Toxicity	Other Grade 3-4 Toxicities		Emetogenic potential
Pemetrexed + Cisplatin N=839	Neutropenia	15.1%	5.6%	Febrile Neutropenia	1.3%	Level 5-4
				Alopecia (any grade)	11.9%	
				Thrombocytopenia	4,1%	
				Nausea	7.2%	
				Vomiting	6.1%	
				Fatigue	6.7%	
				Dehydration (any grade)	3.6%	
				Transfusions	16.4%	

After being collected the desired information, it was necessary to structure the way AE should arise in the computer system to be recorded. It was intended that the notification was carried out in a simple and consistent way in all registers. In this sense, in addition to standardizing the definition of AE, it was also desirable to involve the possible degrees of damage caused. For this purpose, based on the Common Terminology Criteria for Adverse Events (CTCAE) v4.3 from National Cancer Institute (NCI), I elaborated and proposed the layout shown in table 10 to be inserted into the computer system, where each AE is defined and its severity is graded into levels one to five (44). Thus, the health professional begins by typing the name of the incident in a field intended for this purpose. After, the name is recognized as an existing term in the database, and automatically arises the definition of AE and characterization of each of the five degrees of damage. Then, the professional simply choose a level of severity of the event. With this format, it becomes easier for the professional notify the AE and, moreover, reduces human error because it minimizes the use of free text fields and the introduction of bias in the input data (eg. different designations and classifications).

Table 10 - Suggested layout for AE section of the computer system, with the example of anemia.
(LLN – Lower Limit of Normal; Hgb – Hemoglobin)

Adverse Event	1	2	3	4	5
Anemia	Hgb <LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN - 100 g/L	Hgb <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 - 80g/L	Hgb <8.0 g/dL; <4.9 mmol/L; <80 g/L; transfusion indicated	Life-threatening consequences; urgent intervention indicated	Death
Definition: A disorder characterized by an reduction in the amount of hemoglobin in 100 ml of blood. Signs and symptoms of anemia may include pallor of the skin and mucous membranes, shortness of breath, palpitations of the heart, soft systolic murmurs, lethargy, and fatigability.					

Although this work was carried out in november 2015, this information was not immediately integrated into the system because the computer module intended for chemotherapy had not yet been developed. Thus, this work remained in standby mode to be incorporated later during the software building process.

After I developed this work oriented to the chemotherapy regimens, Prof. Francisco Pimentel suggested to expand it to radiotherapy, in order to put the system into practice, since Lenitudes MC&R was already receiving several patients for radiotherapy purpose. In this sense, I initiated a detailed research on the AE more frequent in radiation treatment.

Since this is a localized therapy, it is essential to take into account many factors that influence the onset of AE: the irradiated anatomical area, the technique used and the radiation dose to which the patient is exposed. In a generic way the possible AE, acute and late, were grouped taking into account the location of the irradiated tumor and anatomical area (table 11).

Table 11- Acute and late AE caused by radiation, by anatomical location of the tumor (18,19).

Area	Anatomic location	Acute AE		Late AE	
CNS	Brain	Earache Headache Nausea	Alopecia Brain edema Radiodermitis	Hypoacusis Chronic otitis Pituitary dysfunction	Cataracts Radionecrosis
	Others				
Head and neck		Odynophagia Dysphagia Dysphonia Xerostomia Dysgeusia	Weight loss Radiodermitis Mucositis Alopecia	Subcutaneous fibrosis Skin ulcerations Necrosis (soft tissues, cartilage, jaw) Odynophagia/Dysphagia/ Persistent dysphonia Slow healing	Fistulation Fall dental parts Chronic otitis: hypoacusis Apical pulmonary fibrosis Myelopathy
Chest	Breast	Odynophagia Dysphagia Dysphonia Dyspnoea Cough Mastalgia	Pneumoniae Pericarditis Myocarditis Radiodermitis Cytopenia	Breast retraction Lymphedema brachial Endocarditis Myocardial infarction Osteonecrosis costal Pulmonary fibrosis	Dyspnoea Chronic cough Esophageal stricture Chronic pericarditis Myelopathy
	Lung				
	Others				
Abdomen and Pelvis	Urology	Nausea Vomiting Abdominal pain Diarrhea Pollakiuria Dysuria	Nocturia Cytopenia Rectal tenesmus Proctitis Sigmoidite Radiodermitis	Scrotal edema Rectal stricture Colonic perforation or obstruction Bladder retraction Urinary incontinence Chronic cystitis Vesico/vaginal fistula Rectum/vaginal fistula Vaginal retraction	Lymphedema of the extremities Changes in menstrual cycle Sterility Impotency Liver disease and nephropathy
	Gynecology				
	Colo-retal				
	Others				
Skin and extremities		Erythema Dermatitis	Radiodermitis	Subcutaneous fibrosis Lymphedema in extremities Anchylosis	Necrosis of the bone and soft tissues

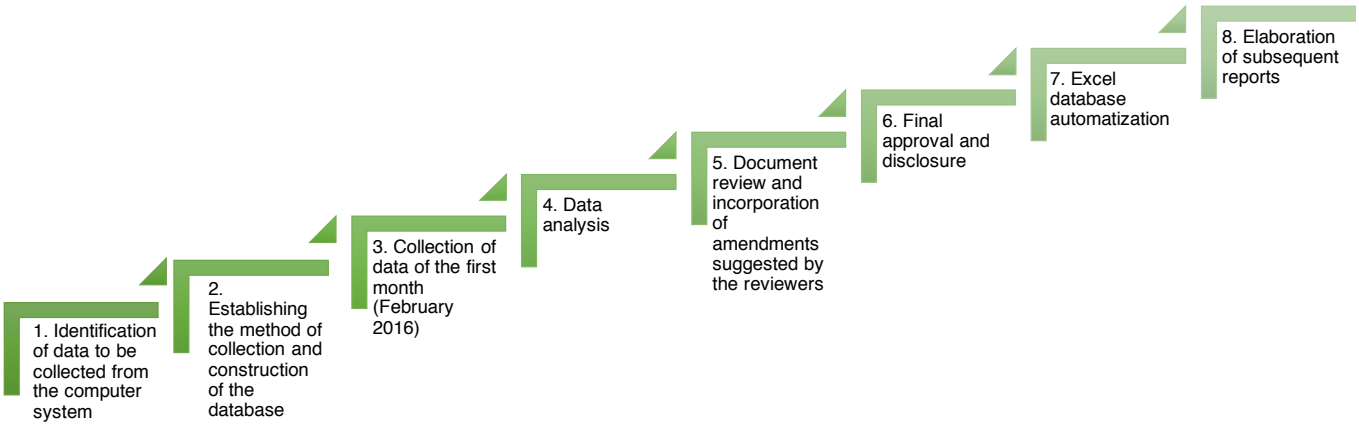
Similar to what happened with the chemotherapy regimens, it was necessary to search for a specific classification for the damage caused by radiation, in order to standardize the notification of the AE. The classification adopted was Acute & Late Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) Radiation Toxicity Grading which also includes five levels of damage caused (45). Aside from being one of the most used classifications in this area, the module MOSAIQ Radiation Oncology used in Lenitudes MC&R already contained a section for the

AE register through this classification. Since there was already a tool for this purpose, there was no need to integrate a new database with the definition/classification of AE. Thus, the research conducted served to alert and raise the awareness of professionals about the incidents associated with this type of treatment, and served as a theoretical support for the preparation of the AE monitoring reports presented in the next section.

3.1.6 AE monitoring periodic reports associated with radiotherapy

Once performed a literature review regarding the most common AE associated with radiotherapy, I proposed to apply this work to clinical practice and monitor the reporting of AE in the internal computer system. The data obtained from monitoring records made by health professionals was the basis for the preparation of periodic reports. This was a dynamic process which required to overcome several stages, from design to conception, extraction of data to their interpretation. Since the initial phase up to the stage of structuring and validation of the report format, the help of Dr. Fernando Costa, radiation oncologist physician in Lenitudes MC&R, who accompanied me throughout all the process, was essential. The various steps are shown schematically in figure 11.

Figure 11 – Representative scheme of the process of developing periodic reports of AE monitoring.



The first step in this process was to identify the information necessary to collect of the computerized system to perform a robust analysis of the data. In addition to the type of AE and its severity, other elements were essential, such as patient demographics (age and gender), the type of cancer (location and histology), stage of cancer, the radiation therapy technique used (TT 3D CRT, VMAT), the intent of treatment, number of sessions and the conducting of chemotherapy (prior or concomitant). All these data were available and accessible in the medical record software.

1. Once the fields of interest identified it was necessary to create a database to store them. To this end, I created a Excel registry base with all these parameters. The next step was to define how this information would be collected from the MOSAIQ software. For this purpose, I prepared the SOP for "Collection of AE's information on MOSAIQ® Oncology Information System software" (see annex V). This SOP describes, step by step, the data collection method and the process of filling the fields created in the database.
2. After defining the method of collection and registration of the information, it was time to put into practice the procedure and collect data from the first month of radiotherapy activity (February 2016). Over several days the data of each patient followed in radiotherapy during that month were introduced, featuring in detail all the required fields.
3. After the construction of the database it was necessary to analyze and interpret the information obtained. In this sense, I elaborated the SOP for "Development of AE periodic report", where I described orientations for the construction of the document, divided into three sections:
    a. Drafting of the report – purpose of preparing the document, who is responsible for its production, which tools are used;
    b. Report structure – header, contextualization, statistical data analysis, conclusion and tables-summary (monthly and semi-annual);
    c. Report disclosure policy – periodicity of the report, date and method of dissemination to the employees of Lenitudes MC&R.

    Based on this SOP, I performed the data analysis, developed charts and graphs showing the distribution of the different AE by cancers, radiation technique and treatment intentions. The main objective of this statistical analysis was to compare the results obtained in Lenitudes MC&R to the findings in the literature. This analysis was also important to realize which areas can benefit from an improvement in the approach to treatment, or the techniques that exhibit better results compared to predicted in the literature.
4. After performing the analysis of the results and drawing conclusions about the month of treatment, the written document went through two stages of review: one for the radioncologist and other for the clinical director of the unit. These reviews were essential to set what terms to use, define the most appropriate structure to present data

or add different conclusions. Once the areas for improvement were identified, I introduced the changes to the document with the noted suggestions.

5. After the changes suggested by the reviewers, the document “followed” for approval of the administrative board of Lenitudes and was disclosed for the whole team involved in the radiotherapy unit of Lenitudes MC&R.
6. Once the final structure of the report defined and approved, it was necesssary to automate the data analysis in order to facilitate the treatment of large amounts of information. Over several days, I explored the different formulas in Excel “looking for the best” to each scenario. In this way, the calculations inherent to the statistical analysis is performed rapidly and automatically, which reduces human error.
7. After all this process became systematic, periodic reports of subsequent months were developed and disseminated by the team, as established on both procedures.

During the internship period I prepared reports of radiotherapy treatments that were carried out during the months of February, March, April and May 2016 (see annex VI). The main objective of this activity was to gather the available information about the AE associated with radiotherapy treatments performed, in an attempt to identify possible areas which need improvement or require greater vigilance. Over the months, it was concluded that AE are suited as expected in the literature with regard to the causality of the events. The most reported AE was the radiodermatitis. The analysis was made based in the incidence of AE by type of cancer, age of patients, for performance or nonperformance of chemotherapy in combination, or by type of radiotherapy technique used. The balance was positive, especially in patients undergoing VMAT technique that is less invasive. When compared to technical TT 3D CRT, the VMAT led to the appearance of a smaller number of AE in patients treated. The fact that the numbers are positive due in large part to the care provided to the patient, the teachings transmitted in the nursing consultation, and the adequacy of radiation therapy techniques used in each case.

3.2 Multidisciplinary Activities

As mentioned earlier, although the R&D unit was taking the first steps at the beginning of my internship, I had the opportunity to collaborate on some tasks in this area. These activities were developed during the entire time of internship and I will describe them in more detail in the following sections.

3.2.1 R&D

3.2.1.1 Project Management & Medical Writing

In addition to the activities that were performed within the risk management system, I collaborated in some other projects as medical writer and project manager.

One of my first assignments was to collaborate in the elaboration of a program for workshops promoted by Lenitudes MC&R and Eruditus. The goal was to organize a serie of workshops related to the theme of immuno-oncolgy, directed to medical oncologists and pulmonologists. Initially there were designed two workshops related to lung tumors and liquid tumors (lymphomas and leukemias). I gave my contribution conducting bibliographic research on similar programs that had already been made, trying to identify the key issues as well as renowned speakers in the area. Subsequently, with the information collected in a teamwork, we defined the agenda of the first workshop. A considerable amount of time for compilation of information and organization of agenda reflected the care that was taken into account for its preparation.

I also collaborated in another project named 'Neways: Cancer Network for Aging Welfare'. This project intends to discuss two of the great problems of our society: the progressive aging of the population and the high incidence of cancer after 65 years. Concerning this scenario, there is an imperative need to integrate geriatric skills in the treatment of cancer in elderly and adapting the therapeutic strategy to the nature of senior individuals. Therefore, this project aims to discuss this subject at national level, and to develop activities to improve or optimize the portuguese reality. I had the opportunity to participate since the beginning of this project, witnessing all meetings and elaborating the minutes of some of these meetings. I collaborated in the organization of the first meeting of the steering committee, which marked the official start of the project. At the first meeting, there was established the mission and objectives of the project, its image and name. After that, I gave a major contribution in writing an editorial in the "Acta Médica Portuguesa",

which was developed in order to disseminate the principles of the project within the medical community:

- Pimentel FL, Oliveira C, Soares J, Veríssimo M. Neways: Cancer Network for Welfare Aging. Acta Med Port. 2016;29(4):235–6.

Simultaneously, I was also involved in project management and medical writing activities in the context of a clinical study with the intervention of MD. This clinical study arised from investigator initiative, a cardiologist of Lenitudes MC&R, and I collaborated with R&D team in project management, namely in distribution of functions and scheduling of tasks. In regard to my connection to the area of risk management and pharmacovigilance, I was responsible for writing the chapter "Safety Monitoring" of the protocol of this study. I also elaborated the forms for reporting SAE and pregnancy, necessary for this and other future clinical studies. The first need in the beginning of this task was to understand how to build these protocols sections. For this, I searched in the biomedical literature for examples of clinical trial protocols to serve as an example of what I wanted to do. This allowed me to gain knowledge about the various steps in the elaboration process of these important documents. In addition, I also had the opportunity to apply some knowledge in statistics, helping to calculate the sample size required for this clinical study. The sample size calculation was made with the help of the software G*Power 3.1®.

Although R&D has not been the core activity of my internship, due to the phase of development and growth of the unit, these activities were very enriching, allowing me to have different perspectives of the work that can be done in this area.

3.2.1.2 Analysis of investigation fund opportunities for Lenitudes MC&R

During the time I was in Lenitudes MC&R, I was several times requested to search for research opportunities which fitted in the profile and mission of the unit. One of the projects for which I searched research opportunities was the Worldwide Cancer Research Fund, which intends to fund scientific research that may, in the future, help reduce the incidence of cancer or improve cancer survival. For this, I read the information available on the website of the initiative and its own regulations. I tried to identify the requirements of the projects, the applications dates and see if any of the ongoing projects in Lenitudes MC&R was appropriate for the application in the initiative.

Also in the sense of looking for research scenarios, I had the opportunity to participate in the Info Day Research and Innovation Staff Exchanges (RISE), held on 25th of january

2016, in the Academy of Sciences, Lisbon. This initiative intended to present the RISE Marie Sklodowska-Curie Actions (MSCA) program inserted in Horizon 2020, and to clarify potential doubts about it. The MSCA RISE constitute support for mobility and secondment of employees in the area of research and innovation. It enables the creation of partnerships between academic and non-academic institutions, in countries of Europe and other countries. Although it has not made any immediate opportunity for Lenitudes under this initiative, the fact of knowing the main advantages and program incentives, the criteria for evaluation of the application, the funding conditions and the application dates, allowed to be aware of the future projects of Lenitudes that can be appropriate for this initiative.

I also had the opportunity to participate in a clarification session on the legal and financial aspects of the opportunities Horizon 2020, for 2016/2017 calls. This session, occurred on 6th of may 2016, was very enlightening since were presented a number of specific funding opportunities for the area of health, allowing the start of the designing of application hypotheses for Lenitudes MC&R.

3.2.1.3 Clinical research coordination

As a result of above-mentioned topics, during my internship I began to develop some initial work as a clinical research coordinator.

I had the opportunity to attend a study initiation visit training, from a multicenter clinical trial phase 3, in the area of Alzheimer's disease. In Portugal, it will only be conducted one arm of the study, and the Lenitudes MC&R will serve as a unit of support to centers in the northern part of the country, for diagnostic tests performed during the screening phase. Due to the PET-CT equipment, the unit is able to perform these tests that represent one of the steps to check that patients can be eligible to participate in the study. On this visit, the monitor of the Contract Research Organisation (CRO) involved went to the unit and provided training to the research team about their role on the study, the procedures which needed to be performed and their execution times. I occupied the back-up function of the study coordinator. Whenever required, it is my job to establish the connection between the monitor, the clinic and the coordinators of the other research centers and perform scheduling of examinations of patients, depending on the prior order of the radiopharmaceutical. It was the first time that I had the opportunity to witness one such visit and was extremely interesting to see how these visits are performed in practice.

In addition, I still participated in the review of protocols and financial arrangements, accompanied and collaborated in the organization of documentation and in contact with all stakeholders involved, including the other members of the research team, monitors and coordinators of other centers. Despite of not being a function directly related to a clinical research coordinator, I also collaborate in the development sketch for the clinical research laboratory. This is a very important component of development of the R&D unit, since it is crucial to ensure the essential conditions for the proper functioning of clinical research activity according to good clinical practice defined by the ICH. Thus, the clinical research office should contain:

- Space for archives and for storage the kits (material, bottles for sampling);
- Workbench for transfer of patient samples;
- Centrifuge;
- Fridge/freezer;
- Work space.

This was a challenging task since it allowed to go beyond my area of training and give my contribution to define the best working conditions for space where will be performed the clinical research activities.

3.2.2 Quality management (SOPs)

In addition to all the activities already described, I still had the opportunity to collaborate on some tasks related to the Quality Management. My main contribution was the development of SOPs, either under the Risk Management area or in more general fields. In addition to the development of the two SOPs related to the AE periodic monitoring reports mentioned above - "Collection of AE information in MOSAIQ Oncology Information System software" and "Development of AE periodic report" - I still had the function to develop a SOP regarding the processing of MD - "Circuit of delivery of MD for sterilization in out-sourcing". This procedure is also in accordance with standard of documentation control and presents a review periodicity of a year. This is also an important document, taking into consideration that the clinic was in a phase of establishing links with other companies to request services that could not be made centrally. In this sense, define how the DM are delivered to be sterilized in outsourcing is critical at this early stage.

4. Training Sessions

- **II Quality Journeys of CHEDV – 11th November 2015**

In this training there were addressed areas such as risk methods, hospital quality or quality indicators in the control of infection. The intervention of Prof. Dr. José Fragata about risk management was the one that most captivated my interest, both for the subject itself and by the unmistakable experience of Prof. Fragata in this area. The approach to improve procedures as opposed to solely focus on the errors of the people, promotes a culture of safety in which all can do more, better and safer. It was also very interesting the approach to the National Health Evaluation System (*Sistema Nacional de Avaliação em Saúde* – SINAS in portuguese) promoted by the Regulatory Authority of Health (*Entidade Reguladora da Saúde* – ERS in portuguese). This system arises as a result of concern for the right of citizens to access information regarding the quality of health services, promoting more informed decisions, and to continuously improve the quality of care.

- **Course Drug Safety – 4th and 5th of March 2016**

As the main focus of my internship was the risk management area and pharmacovigilance, was of my interest conduct specific training in this area. In this sense, I was informed of the realization of the course "Drug Safety" promoted by UNAVE and immediately was interested in participate. In this course, were discussed topics such as quality healthcare and patient safety, the safety of the medication (medication errors, drug interactions, Look-Alike Sound-Alike (LASA) drugs, high alert drugs or high risk, therapeutic reconciliation) and pharmacovigilance and risk management. Given that the theoretical learning of this matter was entirely autonomous from the start of the internship, it was extremely important and enriching to conduct a training focused to my area of work. I had the opportunity to ask specific questions that appeared during the months of internship, I consolidated the knowledge that I acquired through literature and, above all, I strengthened my passion for this area.

- **MOSAIQ Medical Oncology Training – 29th Feb to 3rd Mar; 16th, 17th Mar 2016**

As mentioned earlier, during my internship, Lenitudes MC&R was under development in several areas. One of them concerned the computer software for use in the oncology unit and day hospital. Thus, as at this point I had already developed the project on the main AE associated with the frequent chemotherapy regimens for the most common cancers, it was

suggested that I attend the training to understand how to integrate the work already performed. The software in question is called MOSAIQ Medical Oncology and was presented to the team in two stages: one week of basic training, where we were taught the main features of the system, and two days of advanced training in system configuration. The training was rewarding once I had the opportunity to realize how a clinical information system it is set up and, on the other hand, I could learn more about the existing functionality in the system for AE's registration.

- **Oncology Spring Meeting – 7th to 9th of April 2016**

The binding of Lenitudes and medical oncology area is assumed. For this reason, in April 2016 I was given the opportunity to participate in the national Oncology Spring Meeting that takes place every year in Evora. Among the wide lot of interesting conferences, I chose to watch those who most identified with my internship route, including lectures on "risk management" or "radiation toxicity management" (mucositis, for example). Besides the themes are very interesting and up to my expectations, it was very gratifying to have the opportunity to participate in an event of this magnitude and importance at the national level.

- **Meeting about Clinical Trials, Health Cluster Portugal – 20th April 2016**

Although the R&D unit is not yet in full operation, the Lenitudes MC&R has always shown interest in embracing the area of clinical trials, as soon as the required conditions were met. In this context, I attended to the Meeting about Clinical Trials sponsored by the Health Cluster Portugal, in Braga. It was a highly enriching day, where were discussed extremely important issues for a center of clinical trials that want to start taking the first steps, such as the main characteristics of excellence centers and the major research opportunities. I believe that the presence of Lenitudes in this meeting was an added value to show the motivation and interest in this area and, on the other hand, to be able to have perception of the key factors for success in clinical trials.

- **ICH Good Clinical Practice (GCP) – 21th April 2016**

Once I have performed some functions related to R&D department, where I collaborated in medical writing and project management it was necessary to perform a course of ICH GCP. Furthermore, as Lenitudes MC&R will participate in some clinical trials, particularly in carrying out the PETs needed, it is required that all members of the research team are trained on GCP.This online course, sponsored by Roche, provides a training focusing on

guidelines for researchers and research team regarding the conduct of clinical practice according to the standards of quality and ethics.

- **Training in Radiation Protection and Safety – 16th May 2016**

Since the Lenitudes MC&R performs activities in the fields of nuclear medicine, imaging and radiation therapy, it is required to complete an annual training about radiation protection and safety, for all employees. In this session, held in Lenitudes facilities, were presented the various types of radiation that professionals of this unit could be exposed, the radiation sources, the protective measures we have to take and the dose limits set by law.

- **International Day of Clinical Trials - Clinical Trials Investigator Initiative, PtCRIN – 25th May 2016**

As a way to commemorate the international day of the clinical trials, PtCRIN organized an event about clinical trials with investigator initiative, which I attended in Infarmed in Lisbon. The main objective of PtCRIN is the implementation, development and organization of the national infrastructure dedicated to clinical research, in line with the national health strategy and harmonized with European standards. In this sense, this session was developed in order to present some funding opportunities in Europe for clinical trials, highlighting the role of interventional studies with MD and the importance of the training of the research team in GCP.

5. Discussion

This section present the main obstacles and difficulties faced, as well as the most positive aspects of this journey.

Even before starting my internship, I had the opportunity to meet the clinical director of Lenitudes MC&R where it was explained to me that the clinic was still in a start-up phase of its activity. This meant that the internship cannot be conducted only within R&D projects or clinical trials, since the structure was not prepared for it. Thus, I was proposed to develop a stand-alone project in another important area for the clinic: risk management and pharmacovigilance. This proposal came about because, in my first interview, I confessed that this was one of my elections area. I had my first contact with this area in the degree in Biomedical Sciences, in the curricular unit of clinical pharmacology, with a collaborator of the north pharmacovigilance unit. Soon there began to arise my interest in the safety area. To ensure that my interest in this field was true, I participated in a pharmacovigilance intensive course in the pharmacovigilance unit of Lisbon and '*Vale do Tejo*' in 2014. If this training had already confirmed my desire to trace my journey in this direction, the module "Risk Management and Pharmacovigilance' of the master, held in Infarmed, came to end all doubts. I think the importance of ensuring the safety of drugs developed, as well as the safety of care, is an essential factor for the development of better health care. On the other hand, I think that my interest in this area is also due to my own personality. Of my nature, I am a person who prefers to have perception of the probability of risk or failure, in order to better prepare my interventions and reduce this possibility to a minimum. As such, I try to be proactive and identify what can go wrong before it happens. This is one of the fundamental pillars of risk management: identify and assess risk situations and try to avoid them.

When I was proposed to perform my internship at Lenitudes MC&R, it was explained to me that this was an area that was missing to be develop and, therefore, I had the opportunity to begin to sketch from scratch. If on one hand I was delighted with the proposal, on the other hand I felt immediately a huge responsibility because I had no experience in the area, bringing in with me only the knowledge of previous training and appreciation for the area.

The first three months of the internship were simultaneously the most difficult and the most challenging. Given that there was practically nothing done in this area in the unit, and there was no one trained in risk management, the first months demanded of me an exhaustive literature search. I tried to understand what is risk management, how the other

health units had organized its risk management systems, which methods used and how I could begin to trace the route of Lenitudes in this area. The tools provided by the Problem-Based Learning method (PBL) during my academic training were essential to overcome these dififuldades. Thanks to PBL, I developed soft skills that were extremely important at this beginning of the internship: autonomy, research tools, critical thinking and problem-solving skills. Thus, I faced this opportunity as a way to learn more about it and immersed myself in scientific articles about risk management, books and national and international standards that enabled me to acquire the knowledge necessary to start the project. The first major application of this research was the development of risk management manual of the Lenitudes units. I immediately realized the importance of this document, which assumed the clinic's position towards the safety of care, and its attitute against the risk. In this regard, I tried to compile the basics of risk management, introduce some theoretical concepts and suggested some approaches that, in my view, suited the Lenitudes strategy. The fact of having no expert colleague in this area in the unit and consequently I do not have anyone to consult and confirm my interpretations, conveyed me some insecurity in the beginning. However, over time I was having more confidence in the work performed. A crucial factor to consolidate the idea of being in the "good way" was the fact that the topics addressed in ‘Drug Safety’ course (referred to in section 4) are the same as the study materials that served as the basis for my training on this theme. This course served as a validation of the proposals that I suggested in risk management manual were according to the ideas defended by the experts in the field. Once completed the manual, the strategy to follow was set. In a natural way, other documents were being drawn up, such as registration forms for the suggested procedures, incident reporting forms and some SOPs.

One of the topics of work suggested at the beginning of my internship was to develop tools for monitoring AE associated with treatments and procedures performed in Lenitudes MC&R. After preparation of the risk management manual, I felt able to advance to this project. Thus, following the guiding principles of the manual, I suggested a reactive approach to monitor AE associated with chemotherapy, reported by health professionals. I did a bibliographical research seeking to identify the main AE recorded in the literature for the most common cancers and, in collaboration with the clinical director, I was building a model for the AE database. However, despite of the fact that the monitoring design was aimed initially to chemotherapy, at the beginning of the 2016 Lenitudes MC&R started with radiotherapy treatments, before the beginning of activity of the day hospital. Thus, taking the opportunity of receiving ten new patients every week, Prof. Francisco Pimentel

suggested to create a database with AE addressed to radiotherapy. This was a challenging activity since it was necessary to conduct further research because I had no knowledge of the most common reactions after treatment with radiation. So I went to this challenge in mind that I had much to learn, since my academic training practically does not focus on this area of treatment. For this, I had the help and cooperation of Dr. Fernando Costa, which proved to be always ready and available to "integrate me" in the radiotherapy universe. Once acquired the basic knowledge to support the monitoring of AE associated with radiotherapy, I began a new phase: the structuring and elaboration of periodic reports for monitoring AE. Throughout this process I came across some difficulties in extracting information from the computer software. The fact that the sections intended for AE registration are not defined at the beginning of the process meant that different health professionals (physicians and nurses) did not use the plataform in the same way – the radiation oncologist physicians registered in the "assessment" section, while nurses registered in the "nursing records" or in paper format). Despite it seems a small detail, the fact that the registration method is not uniform meant that sometimes the AE record, made by different professionals, were not consistent for the same patient. In addition, the use of different rating scales for the same AE became difficult to analyze the registered information regarding to the comparison between records. This was one of the main difficulties that I felt in this phase of the internship. The lack of adequacy of the software tool, namely the absence of crucial fields such as the start and end date of the AE, was a limiting factor for the work that I was doing. However, I identified that it was possible to overcome some of the obstacles just giving adequate information to professionals. So I got in touch with nursing team in order to standardize the scale and the severity of the AE used in the registers and this problem has been resolved. On the other hand, the construction process of the first report also required a lot of time and dedication, with several interventions needed until it was achieved the ideal structure. This writing work and readjustment was done in collaboration with Dr. Fernando Costa, who was giving me indications of what to improve in each version of the document. Once established the definitive format, all subsequent reports were conducted without difficulty. In order to accomplished this, it was also essential the automation of the excel database, so that the statistical data analysis and preparation of graphs and tables were made quickly and without requiring user intervention. After many hours dedicated to this work, I think it was quite interesting to be able to use the computer skills acquired throughout my academic career in clinical practice. I can say that the whole process concerning the preparation of periodic reports, with the constant monitoring of

patient records to extract all the reported AE, interpretation and evaluation of causality, were the most challenging and rewarding tasks throughout this internship. The fact that there was not anything previously defined for this purpose demanded greater responsibility, not only in structuring the preparation method and reporting format, but also in how the results are disseminated among the staff members and how they saw the importance of risk management in a clinical unit.

The fact that the unit is still in the development stage allowed me to have contact with different areas and work on various tasks. Although during the master I have done several works where I put my skills of medical writing in practice, I had some fear that in the real world I could not meet the expectations outlined by my superiors. I think this was one of the positive aspects of my internship, because I had the opportunity to prepare several documents that have consolidated my writing skills, whether they were minutes of meetings of research projects, an editorial in a journal, or simply professionals emails. On the other hand, collaboration in project management was also very challenging because I had no experience in the area. I have acquired the basic knowledge to manage a project, reconcile the various stakeholders and manage the tasks to perform.

I think that I have achieved all objectives previously defined concerning the master's degree and my host organization aims. I contributed to the successful monitoring of AE associated with radiotherapy, occurred during four moths in Lenitudes MC&R. This task not only permitted, month to month, to identify what could be improved, but also allowed the unit to had a record of the AE that occurred since the first radiotherapy treatment. In prospective terms, this information can be very valuable to demonstrate, for example, a minor occurrence rate of AE and the evident quality of services, resulting in increased satisfaction by patients when choosing the unit where they want to perform their treatments. On the other hand, I have a deep understanding of risk management systems and knowledge on some methods adopted by different entities.

On a personal level, I have developed some soft skills that are essential to the professional world, such as the sense responsibility and autonomy, organisation, the time management, attention to details, communication skills and adaptation to clinical environment.

In summary, I can emphasise that having to build this project in an autonomous way, just based on the learning acquired along bachelor and master course, and knowledge obtained through the available literature, made this phase of my academic career most challenging and demanding. I take with me nine months of excellent learning, where I was

able of understanding better my strengths and difficulties. This was one of the most enriching experiences of my academic journey and I will continue to learn more and more, take on new challenges and grow professionally and personally.

6. Conclusion

The assessment of patient safety and health care provided has been the subject of several recommendations over the recent times. The main objective is to promote changes to achieve a higher safety culture, which results in greater patient satisfactio. Thus, have knowledge of incidents occurring in the various medical facilities, identifying the frequency, their causes and impact, is the first step towards this improvement. Taking into account the impact that the AE have in morbidity of patients, it is easy to see that monitoring them is essential for health organizations to seek opportunities for improvement in the quality of health care they provide.

I am pleased for having had the opportunity to do my internship in Lenitudes MC&R and to have developed a project in this area. It was a unique experience that has challenged my autonomy, responsibility, organization and the knowledge acquired during academic education related to risk management, pharmacovigilance and R&D. This was, certainly, one of the most enriching years of my academic career and allowed me to grow and become a more competent professional. In addition, this stage helped me to better understand my interests, my strengths and weaknesses and my profile as a professional in the clinical research area. I also realized that the ability to research, allied to dedication and cooperation with experts are essential tools for achieving success in any task performed.

Therefore, I can conclude that I finish my second year of the Master's course in Pharmaceutical Biomedicine with the feeling of satisfaction of having reached the predefined objectives and developed strong soft skills. Now, I'm ready to do and learn more, enjoy all given opportunities and face the world of work.

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Annexes

Annex I - Risk Management Manual *(first page and some sections presented in this document)*

Lenitudes MEDICAL CENTER & RESEARCH	**Nome do documento:** Gestão de Risco		
	Tipo de documento: Manual	**Nº/Versão:**	**Data da 1ª versão:**
Elaboração em: 18/02/2016	**Revisão em:**	**Aprovação em:**	**Revogação em:**
Por: Ana Rita Marques	**Por:**	**Por:**	**Por:**

Lenitudes
MEDICAL CENTER & RESEARCH

MANUAL
DE
GESTÃO DE RISCO

Documento truncado com informação confidencial.

A importância da Gestão de Risco para as Unidades de Saúde Lenitudes

A gestão de risco diz respeito a um conjunto de medidas estabelecidas para aumentar a segurança e, assim, a qualidade de prestação dos cuidados de saúde. A Lenitudes atribui elevada importância aos processos de gestão de qualidade e, por conseguinte, às atividades de gestão de risco. Desta forma, através da identificação prospetiva das circunstâncias que colocam os doentes em risco e da atuação na prevenção e controlo desses mesmos riscos, é possível atender a um grau de maior exigência e procura por cuidados com níveis de qualidade mais elevados.

É indiscutível que os símbolos de garantia, acreditação e/ou certificação são essenciais para que uma unidade de saúde consiga conquistar o mercado nacional e se expandir para mercados internacionais. A gestão de risco pode auxiliar neste âmbito, dado que a ocorrência de eventos adversos graves nas instituições sugere às autoridades externas (ainda que não prove), que existe uma falha nos esforços para salvaguardar a segurança do doente. Desta forma, a implementação de sistemas de relato de incidentes, enquanto ferramenta de gestão do risco, é fortemente recomendada em todas as instituições que se submetem a processos de acreditação externa, seja através da Joint Comission (JC) ou da Caspe Healthcare Knowledge Systems (CHKS).

A melhoria da segurança da prestação de cuidados evita perdas importantíssimas não só em vidas humanas, mas também em custos económicos para a própria empresa (readmissões hospitalares, medicação para tratamento de eventos adversos, entre outros). Para além disto, o enfoque nesta área pode traduzir-se num aumento da confiança nas unidades de saúde e nos seus profissionais, por parte dos utentes, e também no aumento da motivação dos próprios colaboradores da empresa, contribuindo para um melhor desempenho.

Torna-se, assim, fundamental encarar a gestão de risco e a segurança do doente como peças fundamentais na concretização do conceito de “unidade de referência”, ao procurar melhorar a qualidade na saúde e prestar cuidados de excelência.

Annex II - Standard record for the process of RCA

FORMULÁRIO DE REGISTO – ANÁLISE DAS CAUSAS RAIZ

Este ficheiro deve incluir toda a informação considerada necessária que tenha sido adquirida através do processo de Análise de Causas Raiz (ACR).

Breve descrição do incidente/evento clínico			
Data do incidente	_____/_____ /_____ (dd/mm/aa)	**Hora do incidente**	___:___ (Horas:Minutos)
Nome do notificador		**Serviço**	
Causas Proximais			
Fatores Contribuintes			
☐ I – Fatores do pessoal, comunicação ☐ II – Fatores do pessoal, formação ☐ III – Fatores do pessoal, recursos/carga de trabalho ☐ IV – Fatores do trabalho ou do ambiente, ambiente físico e equipamentos ☐ V – Fatores organizacionais ou do serviço, protocolos e procedimentos ☐ VI – Barreiras			
Recomendações de medidas a tomar para evitar a recorrência do incidente			

Notificado por: _____ **Data:** ____/____ /____ (dd/mm/aa)

Assinatura: _____

Annex III - Standard record for the process of the identification and assessment of risk

FORMULÁRIO DE REGISTO – IDENTIFICAÇÃO E AVALIAÇÃO DO RISCO

Este ficheiro deve incluir toda a informação considerada necessária que tenha sido adquirida pelo processo de identificação e avaliação de risco, de forma a documentar o risco em análise.

Data: ____/____ /____ (dd/mm/aa)

Designação do Procedimento/Dispositivo Médico: _____

Classe de Risco de Equipamento (se aplicável):_____

Perigos identificados:

_____

_____

Consequências (C)	**Probabilidade (P)**				
	1	**2**	**3**	**4**	**5**
	Raro	Improvável	Possível	Provável	Quase certo
5 Catastróficas	5	10	15	20	25
4 Maiores	4	8	12	16	20
3 Moderadas	3	6	9	12	15
2 Menores	2	4	6	8	10
1 Insignificante	1	2	3	4	5

1 - 3	Risco baixo
4 - 6	Risco moderado
8 - 12	Risco alto
15-25	Risco extremo

Risco atribuído: (C x P) = ___ x ___ = ___

☐ Risco baixo ☐ Risco moderado ☐ Risco alto ☐ Risco extremo

Risco extremo	Ocorrência quase certa, pelo menos uma vez, nos próximos três meses.	Necessárias medidas corretivas imediatas. Revisão semanal
Risco alto	Ocorrência provável, pelo menos uma vez, nos próximos 4-12 meses.	Necessária atenção especial na gestão do caso. Revisão mensal
Risco moderado	Ocorrência provável no período de 1-2 anos.	Responsabilidade da gestão deve ser especificada. Revisão anual
Risco baixo	Ocorrência possível em alguma altura no período de 2+ anos.	Procedimentos de rotina. Revisão se os procedimentos sofrerem alterações.

Medidas de Controlo de Risco:

_____

_____

Notificado por: _____ **Data:** ____/____ /____

(dd/mm/aa)

Assinatura: _____

Annex IV - ADR reporting form

Lenitudes MEDICAL CENTER & RESEARCH

FORMULÁRIO DE NOTIFICAÇÃO DE REAÇÃO ADVERSA MEDICAMENTOSA (RAM)

CONFIDENCIAL

I - Informações do doente

Nº Processo			
Nome			
Data de nascimento	____/____/____ (dd/mm/aa)	Idade	_____ anos
Peso	_____ Kg	Altura	_____ cm
Sexo	☐ Feminino ☐ Masculino		

II - Detalhes da RAM

Data de início	____/____/____ (dd/mm/aa) ☐ Assinalar caso se trate de uma data estimada	Duração da RAM se < 1 dia	___ h ___ min
Descrição da RAM			
Gravidade da RAM[1] [1] Segundo a classificação NCI CTCAE v4.03	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐		
Outcome	☐ Morte	Data de óbito: ____/____/____ (dd/mm/aa)	
	☐ Cura	Data de recuperação: ____/____/____ (dd/mm/aa)	
	☐ Em recuperação	☐ Persiste sem recuperação	☐ Desconhecida
	Sequelas *(qualquer complicação ou dano causado como consequência da RAM)*: ☐ Sim ☐ Não ☐ Desconhecido		

III - Detalhes do medicamento suspeito

Medicamento(s) suspeito(s) *Por favor especifique o nome comercial se tiver conhecimento*	Dose	Frequência	Via administração	Nº de lote	Data de validade	Data de início de toma	Data de fim de toma	Indicações terapêuticas
1.								
2.								
[Criar as linhas necessárias]								

IV - Detalhes de medicação concomitante

Medicamento(s) concomitante(s) *Por favor especifique o nome comercial se tiver conhecimento*	Dose	Frequência	Via administração	Nº de lote	Data de validade	Data de início de toma	Data de fim de toma	Indicações terapêuticas
1.								
2.								
[Criar as linhas necessárias]								

FORMULÁRIO DE NOTIFICAÇÃO DE REAÇÃO ADVERSA MEDICAMENTOSA (RAM)

V – Outra informação relevante

História de RAM semelhante	
Alergias existentes	
Gravidez	☐ Sim ☐ Não
Reexposição ao medicamento	☐ Sim ☐ Não Se sim, observações:

VI – Gestão da RAM

Terapia medicamentosa de suporte *Por favor especifique o nome comercial se tiver conhecimento*	Dose	Frequência	Via administração	Nº de lote	Data de validade	Data de início de toma	Data de fim de toma	Indicações terapêuticas
1.								
2.								
3.								

Hospitalização do doente *(depois da ocorrência da RAM)*	☐ Sim ☐ Não
Considera a RAM grave?	☐ Sim ☐ Não Se sim, por favor indicar o motivo pelo qual a reação é considerada grave (assinale ✓ nas opções que se aplicam): ☐ Resultou em morte ☐ Colocou a vida em risco ou em perigo de morte (segundo opinião médica) ☐ Motivou o internamento ☐ Resultou em incapacidade significativa ☐ Causou anomalia congénita ☐ Requereu intervenção de um profissional de saúde para prevenir a ocorrência de alguma das situações anteriormente descritas.
Trata-se de uma RAM inesperada?	☐ Sim, a RAM não se encontra descrita no RCM ☐ Não
Relação causal da RAM	☐ Definitiva (certa) ☐ Provável ☐ Possível ☐ Improvável

VII – Informações do notificador

Nome			
Profissão		Especialidade	
Número mecanográfico			
E-mail			
Assinatura		Data	___/___/___ (dd/mm/aa)

Annex V - SOP for "Collection of AE's information on MOSAIQ® Oncology Information System software"

Lenitudes MEDICAL CENTER & RESEARCH	**Nome do documento:** Elaboração do Relatório Periódico de Monitorização de Eventos Adversos		
	Tipo de documento: Procedimento	**Nº/Versão: 1**	**Data da 1ª versão:** 25-02-2016
Elaboração em: 25-02-2016	**Revisão em:**	**Aprovação em:**	**Revogação em:**
Por: Ana Rita Marques	**Por:**	**Por:**	**Por:**

1. Âmbito:

- Esta instrução de trabalho aplica-se à Lenitudes.
- A equipa do grupo de apoio técnico de Gestão de Risco da Lenitudes pretende proceder à elaboração de relatórios periódicos de monitorização dos Eventos Adversos (EA) registados pelos profissionais de saúde, associados à radioterapia.

2. Objetivos:

- Definir a estrutura e processo de elaboração/divulgação do relatório periódico de monitorização de EA.

3. Campo de Aplicação/ Destinatários:

- Grupo de apoio técnico de Gestão de Risco.

4. Referências:

- Não aplicável.

5. Definições

- Não aplicável.

6. Responsabilidades:

- Equipa do grupo de apoio técnico de Gestão de Risco.

7. Descrição:

7.1. Elaboração do relatório

- O relatório periódico de monitorização de EA é elaborado pela equipa do grupo de apoio técnico de Gestão de Risco.

- O principal objetivo do relatório é permitir avaliar a toxicidade dos tratamentos de radioterapia, prestados na Lenitudes *Medical Center & Research*.

- A informação para análise é recolhida conforme se encontra descrito no procedimento interno normalizado "Recolha informação sobre Eventos Adversos do software MOSAIQ® *Oncology Information System*".

- A análise estatística dos dados apresentados é efetuada através da ferramenta Excel.

7.2. Estrutura do relatório

- Cabeçalho: indicação do mês e do ano em que os EA foram recolhidos;
- Contextualização:
    - **a.** Número de doentes a serem seguidos em radioncologia, na Lenitudes *Medical Center & Research*;
    - **b.** Número de doentes a realizar sessões de radioterapia;
    - **c.** Média de idades dos doentes (em anos);
    - **d.** Número de doentes por diferentes neoplasias.
- Análise estatística dos resultados:
    - **a.** Número de EA notificados;
    - **b.** Tipos de EA notificados;
    - **c.** Gravidade de EA notificados;
    - **d.** Distribuição dos EA por patologia;
    - **e.** Distribuição dos EA por estadio da neoplasia;
    - **f.** Taxa de doentes com EA vs. doentes sem manifestação de EA.
- Conclusões: avaliação global dos dados – comparação com o que está previsto na literatura para casos semelhantes; apreciação sobre as medidas tomadas e sugestões de medidas a adotar em situações futuras.
- Quadros resumo (mensal e semestral) com informação sintetizada sobre os doentes que concluíram tratamento em cada mês, quantos manifestaram EA e de que tipo.

NOTA: O primeiro relatório (referente ao mês de Fevereiro de 2016) inclui uma secção introdutória ao tema dos EA associados à radiação. Pretende-se, assim, contextualizar os dados que são analisados, de forma a avaliar a causalidade dos efeitos adversos de forma sustentada.

7.3. Política de divulgação do relatório

- O relatório tem uma periocidade mensal, incluindo os registos inseridos na base de dados entre o primeiro e o último dia de cada mês.
- De forma a permitir que os dados registados na base de dados nos últimos dias de cada mês sejam incluídos na análise, o relatório é divulgado até ao dia 15 do mês seguinte.
- O relatório deve ser divulgado junto de todos os profissionais de saúde da Lenitudes *Medical Center & Research*, através de correio eletrónico (e-mail).

8. Periodicidade de revisão:

- A revisão desde documento apresenta uma periodicidade anual, caso não exista nenhuma ocorrência que justifique a sua antecedência.

9. Registo de Revisões: N/A 1ª Versão do documento.

10. Anexos: Não aplicável.

Annex VI - Periodic report monitoring AE in radiotherapy (March 2016)

Lenitudes MEDICAL CENTER & RESEARCH	**Nome do documento:** Relatório periódico de monitorização de eventos adversos em radioterapia		
	Tipo de documento: Relatório	**Nº/Versão:** 1	**Data 1ª versão:** 14/04/2016
Elaboração em: 14/04/2016	**Revisão em:** 15/04/2016	**Aprovação em:** 15/04/2016	**Revogação em:**
Por: Ana Rita Marques	**Por:** Dr. Fernando Costa (Médico Radioncologista)	**Por:** Prof. Francisco Pimentel (Diretor Clínico)	**Por:**

Lenitudes
MEDICAL CENTER & RESEARCH

RELATÓRIO PERIÓDICO DE MONITORIZAÇÃO DE EVENTOS ADVERSOS EM RADIOTERAPIA

MARÇO DE 2016

Documento truncado com informação confidencial.

O presente relatório apresenta a seguinte estrutura: contextualização; distribuição dos doentes por tipo de neoplasia e tipo de técnica de radioterapia utilizada; análise dos registos de eventos adversos (geral e por área anatómica); conclusão; quadro-resumo mensal e semestral.